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The American Heart Journal

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The American Heart Journal

VOL. 10 OCTOBER, 1934 NO. 1

Original Communications

INVESTIGATION OF THE PATENCY OF PERIPHERAL ARTERIES*

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ARTERIAL PALPATION

ONE of the most important methods for the study of peripheral vascular diseases is the palpation of the arteries of the extremities.† In the arm the brachial, radial and ulnar arteries are easily palpable; in the leg the femoral, posterior tibial, and dorsal pedal arteries usually can be palpated without difficulty. The palpation of the popliteal artery is more difficult; pulsations may not be felt in this artery even when the arteries of the feet show normal pulsations. It is a widely accepted opinion that absence of pulsation in these arteries does not occur in normal individuals, or at least occurs very rarely. This opinion is not wholly justified by a study of the literature. Only a small number of investigations has been published, and there is no agreement on this important question.

Erb investigated clinically 381 persons without manifest arterial disease. He found absence of pulsation in both the posterior tibial arteries in 2 cases; absence of pulsations in the posterior tibial and dorsalis pedis arteries of one foot in two cases. Absence of pulsation in one or more arteries of the feet was therefore found only in 1 per cent of the control cases. Goldflamm investigated 200 persons, but not clinically. He found absence of pulsation in the arteries of the feet in 5 per cent of his cases. Buerger found in 200 persons normal pulsation in the dorsal pedal arteries in all but one case (0.5 per cent); the condition of the posterior tibial arteries is not mentioned in this series.

The agreement between these authors is satisfactory. The results

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†The expression "palpation of arteries" is used hereafter instead of the more correct expression "palpation of the pulsations in arteries."

obtained by Schneyer showed a fundamental difference. A clinical investigation of 500 persons showed absence of pulsation in males in 17 per cent; in females in 29 per cent. It is difficult to give an explanation of this divergence of results. It may be dependent upon differences in the ability to palpate still existing after a long experience with this method.

It is highly desirable to have this problem elucidated by the cooperation of many investigators. The need of an objective method for the control of the palpation is hereby emphasized. The scope of the present investigation was the study of this problem.

OSCILLATIONS

When blood pressure is measured with the instrument of Riva Rocci, oscillations are visible between systolic and diastolic pressure. These

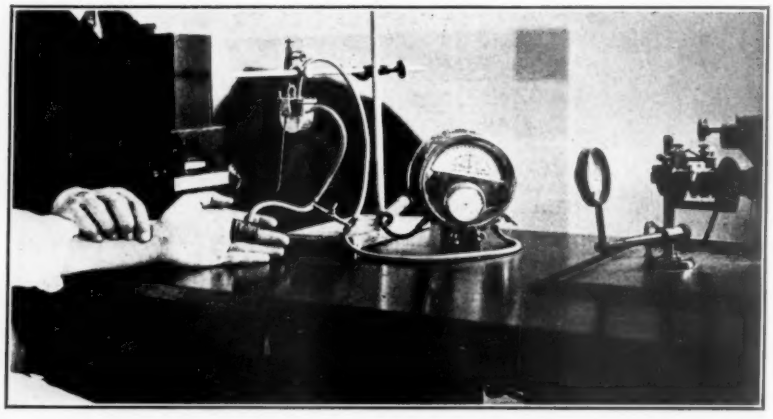

Fig. 1.—Photographic registration of oscillations of the left middle finger with a capsule of Gaertner (see Fig. 2). The oscillograph is suspended in the light beam of a Cambridge electrocardiograph. The capsule in inflated at a pressure of 70 mm. of mercury with the instrument of Pachon.

oscillations can be studied visually, or registered with an oscillograph on smoked paper or a photographic film. In the present investigation an oscillograph of Boulitte, suspended in the light beam of an electrocardiograph, was used (Fig. 1).

It was found necessary to obtain the oscillations of the most distal parts of the extremities. The dorsum of the foot was covered with a small cuff which was fastened around the foot with leather straps. When the cuff was connected with the oscillograph, distinct oscillations appeared.

It was soon apparent that these oscillations were not exclusively from the dorsum of the foot, but also in a small measure from the plantar side. Evidently the systolic expansion was transmitted by the leather

straps to the cuff. When the cuff was fastened on the plantar side again, the oscillations were predominantly but not exclusively from this side. On the hands no good results were obtained with this small cuff. After trying different methods the best results were given by the capsules of Gaertner (Fig. 2). They consist of a hollow metal cone, which is covered with a loose rubber membrane on the inside. This is fastened at the borders of the cone. On one place the cone is pierced and connected with a small metal tube. When the capsule is applied around the finger and the cuff inflated through the metal tube, the space between cone and membrane is filled with air and the membrane is pressed against the finger. If the capsule is connected with the oscillograph, small os-

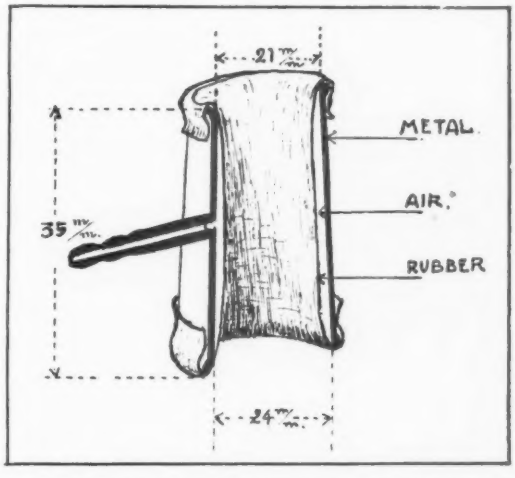

Fig. 2.—Section through capsule of Gaertner. The measurements are those of a commonly used model. Capsules of different sizes are used, according to the diameter of the finger.

cillations from the fingers can be registered. In the same manner oscillations from the arteries of the big toes can be taken with an oval cone.

DETERMINATION OF THE SO-CALLED OCCULT BLOOD PRESSURE BY THE METHOD OF GAERTNER

The capsules of Gaertner, as described above, were originally used for the determination of the blood pressure in a finger. The finger was made anemic by pushing a narrow rubber ring from the end of the finger to the base. Then the capsule was placed over the middle phalanx and inflated above systolic pressure. After the rubber ring was cut, the blood filled the finger up to the capsule. Then the pressure in the capsule was diminished slowly. At a certain pressure there was a sudden filling of the finger tip with blood. At this instant the blood

pressure in the finger was just able to overcome the pressure in the capsule. This pressure was assumed to be the systolic pressure in the finger (Fig. 3).

This method is no longer used for its original purpose, that of determination of the general blood pressure. Changes in the condition of the finger arteries do not allow constant results. Nevertheless this

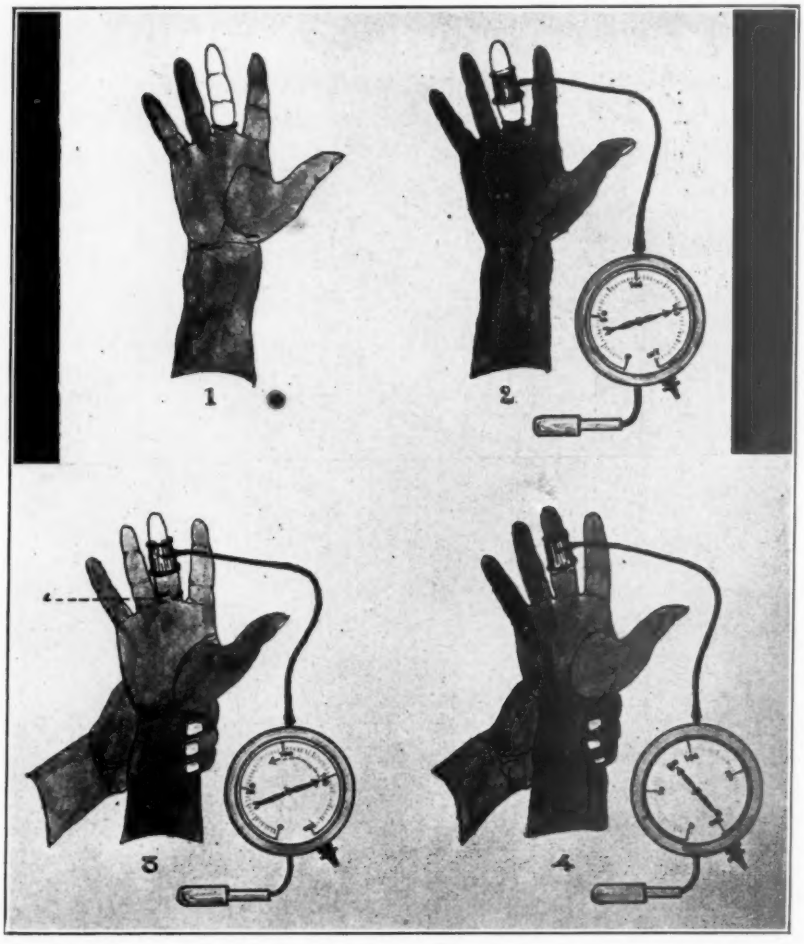

Fig. 3.—Determination of occult blood-pressure with the method of Gaertner.
First phase: A rubber ring is pushed over the third right finger from the end to the base.
Second phase: A capsule of Gaertner, connected with a manometer is placed over the middle phalanx and inflated to a pressure of 150 mm. of mercury.
Third phase: The rubber ring is cut. After this the pressure is diminished slowly.
Fourth phase: At a pressure of 80 mm. of mercury there is a sudden filling of the finger with blood.

method, in the procedure called determination of occult blood pressure, is very useful in the study of arterial diseases. It is the only practical method of blood pressure determination independent of the pulsatory phenomena.

It is quite possible, under certain circumstances that the change from a pulsating blood stream to a continuous stream does not take place, as is usually the case, in the arterioles and capillaries, but in the main arteries.

This possibility was first clearly formulated by L. Bard; he found in a patient with stenosis of the subclavian artery no pulsations on the left side, while the fingers showed a normal occult blood pressure. He assumed that the stenosis of the subclavian artery had abolished the oscillations, without changing the blood pressure. This combination must be considered a rare one. The occurrence of a continuous blood stream is often seen in some diseases, especially arterial embolism, but in most cases there is very marked lowering of the occult pressure.

The occult blood pressure also can be determined at higher levels (ankle, wrist, etc.). In this case the extremity is made anemic by elevation and application of a rubber bandage. The cuff is then fastened around the limb at the level of determination, and inflated above systolic pressure. The bandage is removed, the limb placed horizontally, and the pressure in the cuff is gradually diminished until filling of the distal parts is to be seen. It is not always possible to make an accurate determination, especially in patients with slow circulation, or with irregularities of the pulse (for instance auricular fibrillation). In these cases only approximative values can be obtained.

COMPRESSION METHOD

Normal persons always showed oscillations in most fingers. Sometimes the oscillations were very small or absent in one finger (usually the fifth). These oscillations are derived from the main arteries of the hand, especially the radial and the ulnar artery. The relative significance of these arteries can be found by alternative compression of each of them.

When one of these arteries is closed by an obstructive arterial disease, compression of the other artery will abolish the oscillations in all fingers.

The principle of this method was first used by Allen: When the fist is clinched and the radial artery compressed, there is no filling on opening the hand when the ulnar artery is closed. Only an approximation can be given by this method.

The results of arterial compression can be demonstrated most conveniently in some patients with unilateral arterial obstruction.

CASE 1.—W. S., a man aged forty years, visited the clinic because of whiteness and pain in the fingers. Arterial palpation demonstrated absence of pulsation of the right ulnar and left dorsal pedal artery. Hereupon the arteries were studied with the compression method. The oscillations of every finger were registered under a pres-

sure of 60 mm. of mercury. First the radial artery was compressed; after that the ulnar artery. At last radial and ulnar arteries were both compressed at the same time (Fig. 4).

On the left hand there was no marked change in the oscillations when either the radial or the ulnar artery was closed. During compression of both arteries the oscillations disappeared entirely in all fingers.

On the right hand there was complete disappearance of the oscillations in all

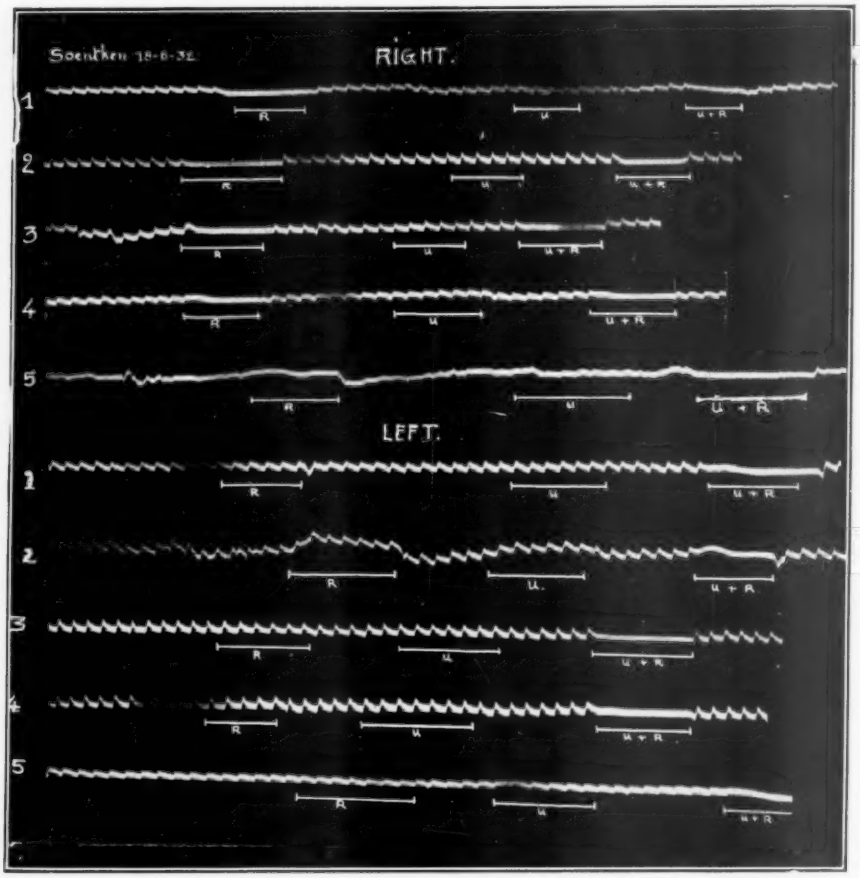

Fig. 4.—Case 1. June 18, 1932. Compression curves of all fingers of the right and left hand.

R = Period of compression of the radial artery.
U = Period of compression of the ulnar artery.
U + R = Period of compression of the ulnar artery and radial artery.

Compression of the radial artery causes a complete disappearance of oscillations in all fingers of the right hand. Occlusion of the right ulnar artery is demonstrated.

fingers when the radial artery alone was compressed. Compression of the ulnar artery had no effect. The conclusion was that at this pressure the oscillations of the fingers came only from the radial artery.

It is possible that oscillations coming from the ulnar artery were present at lower pressures in the capsule. This possibility could be excluded by compression of the radial artery at different pressures (from 80 mm. to 10 mm. of mercury). Always

there was complete disappearance of oscillations when the radial artery was closed. Finally the existence of a continuous blood stream through the ulnar artery was

TABLE I

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. RADIAL ART.	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. ULNAR ART.
R. second finger	40 70*	0	80	75
R. fourth finger	85	0	95	90
L. second finger	30	65	60	40
L. fourth finger	90	100	100	90

	SPONT. OCCULT PRESSURE
R. second finger	
R. fourth finger	
L. second finger	60
L. fourth finger	100

*Value after repetition of the determination (see text).

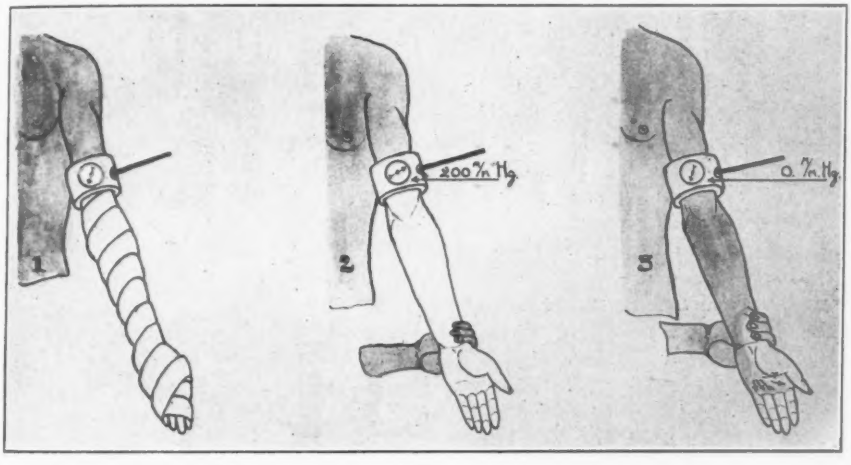

Fig. 5.—Shock method.
First phase: The arm is made anemic with a rubber bandage.
Second phase: A cuff is applied over the upper arm and inflated to a pressure of 200 mm. of mercury. The rubber bandage is taken off.
Third phase: The cuff is suddenly deflated during compression of the radial artery. The blood streams in the lower arm and through the ulnar artery slowly in the hand. The ulnar artery is patent to some degree.

considered. For this investigation the influence of the arterial compression on the occult blood pressure was determined as described above. Before and after every determination with arterial compression the spontaneous occult pressure was determined to avoid errors by variations in the pressure during the investigation. The results obtained in the second and fourth fingers of both hands are given in Table I.

Table I shows that in the left hand compression of one artery (radial or ulnar) caused no, or only a small, lowering of the occult blood pressure. The low value that was found in the first determination in the left and right second finger probably was caused by a contraction of the finger arteries (this very low value for the occult pressure in the first determination was seen also in other cases). On the right hand, compression of the radial artery caused a fall of the occult pressure to zero! So it was proved that the blood stream in the fingers of this hand came almost totally from the radial artery. But with another method, which subsequently is called shock

method, there could be demonstrated a slight permeability of the ulnar artery (Fig. 5). The arm was made anemic by elevation and bandaging, and the circulation was cut off by inflation of a cuff around the upper arm. If the circulation was suddenly released, there was a sudden filling of the right and left arm and hands. When this experiment was repeated with the radial artery compressed, there was a fast filling of the hand on the left side through the open ulnar artery. On the right side there was a sudden filling of the lower arm up to the wrist. In the hand there was a very slow but progressive redness on the ulnar side and gradual filling of the hand and the finger. When the same experiment was repeated during compression of both the radial and the ulnar artery, there was no filling of the hand at the right or left side.

From these experiments the conclusion was drawn that there was still some degree of patency of the ulnar artery.

In the same manner the feet of this patient were investigated, and an almost total occlusion of the left dorsal pedal artery could be demonstrated.

A diagnosis of incipient thrombo-angiitis obliterans was made.

CASE 2.—A. R., a man aged fifty-three years, entered the ward with a diagnosis of luetic aortitis. During physical examination it was found that the left radial artery showed only very small pulsations, while the right radial artery pulsated normally. The pulsations of the left ulnar artery were somewhat smaller than the pulsations of the right. The arterial tension on the left upper arm was 90-55, on the right upper arm 110-55. This small difference did not explain the pulsus differens. The compression method was used for distinguishing between a real pulsus differens and a pseudo pulsus differens, caused by a local lesion of the radial artery (Fig. 6). It was found that the oscillations of every finger on the right side came from both the radial and the ulnar artery. On the left side the oscillations disappeared completely during compression of the ulnar artery. Compression of the radial artery had no effect. This investigation was repeated three times, always with the same results.

The small pulsations that were felt in the left radial artery did not reach the fingers.

The determination of the occult blood pressure gave the results shown in Table II.

TABLE II

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. RADIAL ART.	OCCULT PRESS. DURING COMPR. ULNAR ART.	SPONT. OCCULT PRESSURE
Right second finger	50	30	50	60
Right fourth finger		40	45	65
Left second finger	60	65	0	65
Left fourth finger	65	55	0	70

These results showed that the occult blood pressure on the right side depended upon the radial and the ulnar arteries, while on the left side no occult pressure dependent upon the radial artery was found.

With the shock method it was found that the filling of the hand during compression of the ulnar artery was rather prompt, although slower than on the right side. During compression of both the radial and the ulnar artery on the left side

there still was a rather prompt filling of the hand. It was clear that another artery was responsible for this filling. On the dorsum of the hand a small pulsating vessel was found. Compression of this extra artery together with the radial and ulnar arteries did not prevent filling of the hand, although it was much slower. This indicated the presence of a fourth artery participating in the filling of the hand; this artery could not be localized by palpation of the hand. Patency of the radial artery was not proved or disproved by these experiments.

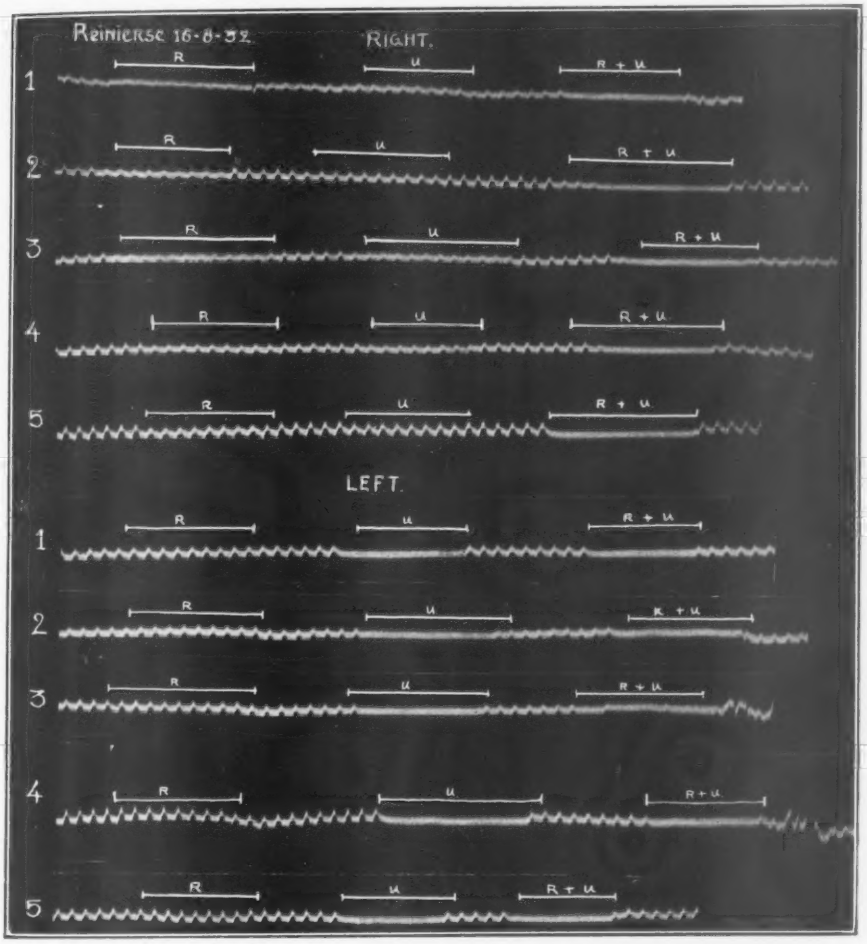

Fig. 6.—Case 2. August 16, 1932. Compression curves of all the fingers from the right and left hand. Compression of the ulnar artery causes a complete disappearance of the oscillations in all the fingers of the left hand. Occlusion of the left radial artery is demonstrated.

On the right side, compression of both the radial and the ulnar arteries prevented filling of the hand. Therefore no extra arteries could be demonstrated here. The normal interosseous artery seemed never to cause a filling of the hand.

The extra arteries on the left side were supposed to be collateral arteries, widened by the occlusion of the radial artery. This occlusion was only partial at the wrist (presence of small pulsation), but a total, or almost total, occlusion must have been present in a more distal part of the artery.

The conclusion was reached that this patient had a pseudo pulsus differens, caused by a local narrowing of the radial artery. The small difference in blood pressure between the right and left upper arms probably had no clinical significance.

The results obtained from examination of the two patients above show a strict agreement between both the compression curves of oscillations and the determinations of occult blood pressure during compression. Sometimes other results were obtained.

CASE 3.—Patient D. J., a man aged forty-seven years, with carcinoma of the stomach, was found to have a very small radial artery on the right side. The right ulnar artery was more developed than the left. Compression curves showed that on the normal left side the oscillations came from both the radial and the ulnar arteries. On the right side the oscillations came exclusively from the ulnar artery (with the exception of very faint oscillations in the right thumb, originating from the radial artery). Determinations of the occult blood pressure were made. (Table III.)

TABLE III

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. ULNAR ART.	OCCULT PRESS. DURING COMPR. RADIAL ART.	DITTO
Right second finger	75	40	I 55	II 70
Left second finger	70	55	I 70	II 80

	OCCULT PRESS. DURING COMPR. ULNAR ART.	SPONT. OCCULT PRESSURE
Right second finger	40	70

Although the oscillations were of totally different composition on the right and the left side, there were no marked differences in the occult pressure.

This case presents an example of absence of pulsation with only slightly lowered occult pressure (right second finger during compression of ulnar artery). This combination was found to be rare.

CASE 4.—Miss V. C., thirty-eight years of age, had been visiting the clinic off and on for several years. She had marked arterial spasm of the Raynaud type in hands and feet; later she developed an extensive scleroderma on the chest and hips.

Arterial palpation showed absence of pulsations in the left dorsal pedal artery. The other arteries of feet and hands showed normal pulsation.

Arterial occlusion is not found in most cases of Raynaud's disease. The patency of the left dorsal pedal artery in this case with the typical clinical picture of Raynaud's was therefore investigated. (Fig. 7.)

Compression curves showed that the oscillations of the normal right foot came from both the posterial tibial and the dorsal pedal artery, with some preponderance of the latter. On the left foot the oscillations came exclusively from the posterior tibial artery.

These curves showed, in agreement with the arterial palpation, that the left dorsal pedal artery was not patent for oscillations. With a capsule especially fitted for the big toe the occult pressure was determined with the same technic as that described for the finger. Owing to technical difficulties the results were not so accurate as those on the finger, but nevertheless quite significant. (Table IV.)

TABLE IV

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. A. TIB. POST.	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. A. DORS. PED.
Right big toe	75	95	90	60
Left big toe	70	0	110	90

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. A. TIB. POST.	OCCULT PRESS. DURING COMPR. A. TIB. POST. + A. DORS. PED.	SPONT. OCCULT PRESSURE
Right big toe	80	85	0	85
Left big toe	95	0		75

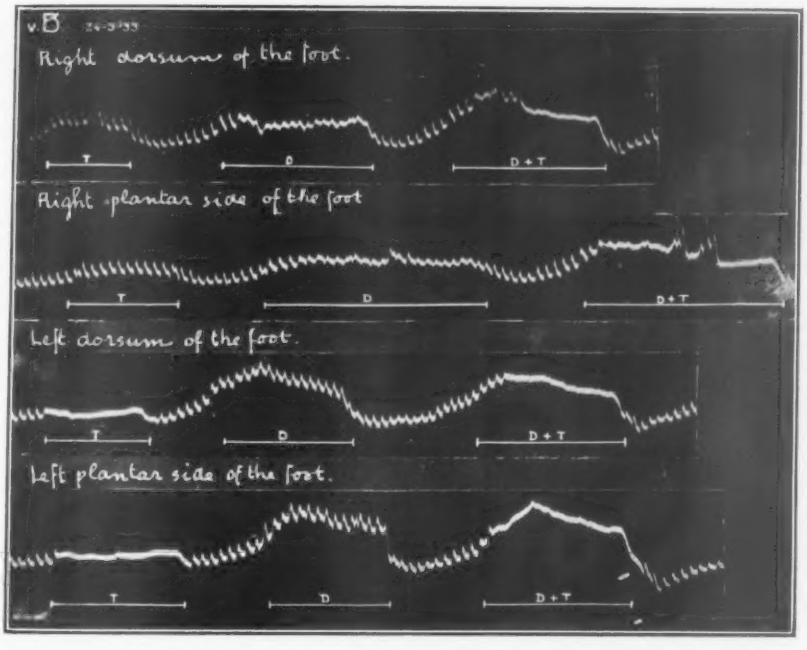

Fig. 7.—Case 4. March 24, 1933. Compression curves of the right and left foot.
T = Period of compression of posterior tibial artery.
D = Period of compression of dorsal pedal artery.
T + D = Period of compression of posterior tibial and dorsal pedal artery.
Compression of the posterior tibial artery causes complete disappearance of the oscillations in the left foot. Occlusion of the left dorsal pedal artery is demonstrated.

These results showed that compression of the posterior tibial artery had no effect on the normal right side, but gave a fall of the occult pressure to zero on the left side. Compression of the dorsal pedal artery had no effect on the left side, slight effect on the right side. An almost total occlusion of the left dorsal pedal artery had to be assumed. Now the shock method was carried out. The leg was made anemic, and arterial circulation was obstructed by a cuff, inflated to 220 mm. of mercury around the upper leg. Afterward the tension in the cuff was suddenly released, during compression of the posterior tibial artery. On the right side there was a prompt filling of the leg and the foot while the toes showed an irregular filling (arterial spasm). On the left side there was a prompt filling of the leg to the ankle. From this point there was a very slow progressive redness of the dorsum

of the foot, which, after two minutes had elapsed, had not yet reached the distal parts. Release of the posterior tibial artery gave a prompt filling of the foot. In this manner a very small degree of patency could be demonstrated in this artery.

The value of the methods described for the clinical investigation of arterial occlusion was proved on different groups of patients.

Compression curves of the hands.

1. In patients with normally pulsating radial and ulnar arteries. In this group curves were made of 24 patients. Arterial compression in these control cases showed some normal variations. Two extreme groups with many intermediate cases could be distinguished. In the first group compression of one artery alone (radial or ulnar) had no marked influence on the oscillations. Here it was evident that in all fingers the oscillations came from both arteries. When one artery was compressed, the other could compensate for the resulting loss of circulation.

In the second group there were differences between the fingers. The oscillation of the thumb and sometimes also of the second finger came only from the radial artery. In the third, fourth, and fifth fingers the influence of the ulnar artery gradually increased. Sometimes the fifth finger showed again a preponderance of the radial artery, especially when compared with the fourth finger.

2. Patients with absence of pulsations in one or both ulnar arteries. In this group 8 cases were investigated. One of these (Case 1) has been described above.

Table V shows that oscillations from the ulnar artery often could be demonstrated in cases which had no palpable pulsations of this artery.

In a case with changes in the patency of the ulnar arteries (No. 8 of Table V) compression curves gave a better insight into the condition of the artery than did arterial palpation. In the first two cases there was complete agreement between arterial palpation and compression curves. The determination of the occult pressure showed also an almost total occlusion. Compression of the radial artery caused a fall in pressure to zero (in both hands of the second case and in the right hand of the first case of the table).

In the other cases the relation between arterial palpation and compression curves was variable.

Determination of occult pressure showed in those cases that were investigated (Nos. 3, 5, and 8) that either the radial or the ulnar artery alone could uphold a good occult pressure in the fingers.

Compression curves of the arteries of the foot.

The influence of alternative compression of the posterior tibial and the dorsal pedal artery on the oscillations of the dorsal and plantar side of the foot was investigated in some groups of patients.

TABLE V

		NAME		DIAGNOSIS	NONPALPABLE ULNAR A.	RESULTANT COMPRESSION CURVES OSC. R. HAND	OSC. L. HAND
1		W. T.	41 years	Thoracic aneurysm	Right	Exclusively from radial A.	Osc. mixed from radial A. and ulnar A.
2		A. K.	72 years	Tabes dorsalis	Both	Exclusively from radial A.	Exclusively from radial A.
3		N. d. G.	32 years	Auricular fibrillation	Both	Exclusively from radial A.	Almost exclusively from radial A. (except faint. osc. thumb)
4		L. F.	47 years	Scleroderma	Both	Exclusively from radial A.	Almost exclusively from radial A. (except faint osc. third and fourth fingers)
5		D. S.	53 years	Sprue	Both	Almost exclusively from radial A. (except faint osc. first, fourth, fifth fingers)	Mixed from radial and ulnar A.
6		H. B.	50 years	Auricular fibrillation	Right	Mixed from radial and ulnar A.	Mixed from radial and ulnar A.
7		C. M.	51 years	Cardiac asthma	Right	Mixed from radial and ulnar A.	Mixed from radial and ulnar A.
8	10/8	C. B.	64 years	Pernicious anemia	Both	Almost exclusively from radial A. (except faint osc. first and fourth fingers)	Mixed from radial and ulnar A.
	5/9				Right	Predominant from radial A. (however, distinct osc. from ulnar A. in all fingers)	Mixed from radial and ulnar A.
	6/9	Fever (temp. 38.4°)			Neither	Predominant from radial A. (however, distinct osc. from ulnar A. in all fingers)	Mixed from radial and ulnar A.
	20/9				Right	Predominant from radial A. (however, distinct osc. from ulnar A. in all fingers)	Mixed from radial and ulnar A.

Control group.

1. Patients with normal pulsations in the posterior tibial and the dorsal pedal artery — 30 cases
   - Oscillations from both arteries present — 27 cases
   - Oscillations from only one artery present — 3 cases

These three cases need a special discussion. In one case the oscillations were too small and indistinct to make the forming of a reliable judgment possible. The second case had a peculiar arterial disease, which was diagnosed as thrombo-angiitis obliterans of the (digital) arteries of the toes. In this case the oscillations in both feet came from the posterior tibial arteries only, although there were normal pulsations in the dorsal pedal arteries. A possible explanation was an obliteration of the principal branches of the dorsal pedal artery. In a third case, with Addison's disease, there were small but distinct oscillations, which came only from the dorsal pedal arteries. The posterior tibial arteries showed normal pulsations. Why these pulsations could not be demonstrated on the foot was not explained.

These results showed that in most cases with normally pulsating arteries of the feet there were on the dorsal and plantar side oscillations from both arteries; exceptionally the oscillations came only from one artery.

2. Patients with absence of pulsations in one or both dorsal pedal arteries.

- *Absence of pulsations in both dorsal pedal arteries* — 9 cases
  - Oscill. *only* from post. tib. art. in both feet — 6 cases
  - Oscill. *only* from post. tib. art. in one foot and predominantly from post. tib. art. in the other foot (with faint oscill. from the dorsal ped. art.) — 2 cases
  - Oscill. from both the post. tib. and dors. ped. art. — 1 case
- *Absence of pulsations in one dorsal pedal artery* — 4 cases
  - Oscill. only from the post. tib. art. of the same side — 3 cases
  - Oscill. from both the post. tib. and the dors. ped. arteries of the same side — 1 case

In nine cases of this group there was strict agreement between pulsations and oscillations. In two cases there was a very slight difference. In two cases there was no agreement. In these latter cases patency of dorsal pedal arteries that showed no pulsation on palpation was proved.

3. Patients with absence of pulsations in one or both posterior tibial arteries.

Absence of pulsations in both post. tib. arteries	6 cases
Oscill. in both feet from the dorsal ped. art. only	2 cases
Oscill. in both feet from both the post. tib. and the dors. ped. art.	4 cases
Absence of pulsations in one post. tib. artery	2 cases
Oscill. on the same side from the dors. ped. art. only	1 case
Oscill. on the same side from both the post. tib. and the dors. ped. art.	1 case

In this group there was striet agreement between pulsations and oscillations in 3 out of 8 cases. In the other cases patency of the posterior tibial arteries had to be assumed, although pulsations could not be felt. Absence of patency for oscillations in the posterior tibial artery seems to be rare in patients without manifest arterial disease.

The following conclusions could be drawn:

1. When no pulsations of the dorsal pedal artery were felt, there were no oscillations from this artery in most cases.

2. When no oscillations from the dorsal pedal artery were found, there were no pulsations in this artery in most cases.

3. When no pulsations were found in the *posterior tibial artery*, often oscillations from this artery could be detected.

These results indicated that the palpation of the posterior tibial artery is less reliable than palpation of the dorsal pedal artery.

The compression method can demonstrate the patency of arteries irrespective of palpation. It cannot prove with absolute certainty the occlusion of arteries. It should therefore be combined with the determination of occult blood pressure and the shock method. The degree of patency of the arteries of the extremities can be estimated with a fair degree of accuracy by the combination of these methods.

SUMMARY

1. A method for the registration of arterial oscillations in fingers and feet is described.

2. This method is used as a test for the patency of the main arteries. By alternative compression of the radial and ulnar arteries on the hand, of the posterior tibial and dorsal pedal arteries on the feet, the composition of the oscillations can be studied.

3. The so-called occult blood pressure in fingers and big toes was studied by the method of Gaertner. The influence of compression of arteries on the occult blood pressure was studied and used for testing the patency of these arteries.

4. A third method, called shock method, was used for testing the patency of almost totally occluded arteries. Most of these arteries were found to have some degree of patency.

5. The relation between the results of arterial palpation and the compression method was investigated in different groups of patients.

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TREATMENT OF CHRONIC HEART DISEASE BY TOTAL ABLATION OF THE THYROID GLAND*†

VII. The Heart in Artificial Myxedema

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STUDIES of the heart in spontaneous myxedema[3, 10, 21, 26, 28, 30, 34] during the past decade have demonstrated that (1) the heart size, as measured by the seven-foot roentgenogram, is increased; (2) the voltages of the P, T, and QRS waves of the electrocardiogram are frequently diminished;[18, 31, 33, 35, 39] and (3) cardiac contractions are less vigorous.[2, 30] Opinions differ concerning the clinical significance of these alterations. Zondek[42, 43] and Fahr[14] maintain that cardiac function is often impaired in patients with myxedema having such changes. Christian,[11, 12] Willius and Haines,[41] Case,[10] Means, White and Krantz,[28] however, studied a total of three hundred patients with myxedema and concluded that heart function is rarely, if ever, impaired. From a recent review of the literature and a comprehensive study of thirty additional cases at the Massachusetts General Hospital, Lerman, Clark and Means[21] conclude that "myxedema heart" in the sense of heart failure occurs rarely, if at all. The studies of the above investigators were confined almost entirely to patients without cardiovascular disease.

In treating patients with chronic heart disease and other conditions by inducing hypothyroidism by total removal of the normal thyroid gland, we have been able to study the development of the cardiovascular changes associated with the development of myxedema. Two aspects of the heart in myxedema have been investigated: first, the character and rate of development of the changes in heart size and electrocardiographic tracings; and, second, the significance of these changes in terms of cardiac function. Studies before, and at varying intervals after, total thyroidectomy have been made in three groups of patients: one group comprising patients with congestive heart failure at the time of, or just before, operation; the second group, patients with angina pectoris; and the third group, patients with no evident functional or anatomical abnormalities. The rationale, technic, and therapeutic results of total thyroidectomy in patients with chronic heart disease and no thyrotoxicosis have been described in previous communications.[4, 8, 9, 15, 16, 37]

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MATERIAL AND METHODS

Thirty-seven patients in whom total thyroidectomy was performed have been studied.* Clinical observations on some of these patients have been reported;[9] observations on the others are to be reported later. The ages of the patients varied from fourteen to sixty-six years; twenty-three were males, and fourteen females. Twenty-two patients showed congestive failure at the time of, or prior to, operation; ten had angina pectoris without congestive failure; one had uncontrollable paroxysmal auricular fibrillation; and four had no cardiovascular disease, the operation having been performed for other reasons. A persistently low basal metabolic rate was obtained in every case after thyroidectomy.

The degree and progress of the hypothyroid state in the subjects of this investigation have been judged by the following indices: (1) basal metabolic rate; (2) velocity of blood flow; (3) serum cholesterol; and (4) clinical observations. Each of these measurements, together with blood pressures and heart rates, was obtained before and at appropriate intervals after thyroidectomy.

The data on the heart size and the electrocardiographic tracings have been analyzed in reference to the degree of hypothyroidism as evaluated on the basis of all these four factors. The postoperative period of study varied in the different patients from one and one-half to twelve months. The earliest postoperative observations on electrocardiographic tracings and heart size were made within the first month after operation.

Teleroentgenograms were taken in the standard manner at the height of inspiration; since appreciable change in the position of the diaphragm may produce apparent changes in heart size. Measurements of the internal diameter of the chest were made to evaluate approximately the position of the diaphragm in successive films. The three standard leads of a No. 2 Hindle electrocardiograph were used. Basal metabolic rate measurements were made in duplicate with a Collins-Benedict-Roth apparatus, and results calculated according to the Aub-DuBois normal standards.[1] The values reported are the average of duplicate analyses which checked within 5 per cent. The preoperative values represent the average of several such measurements on different days. Measurements preoperatively and during the first three to six postoperative weeks were made while the patient was in the hospital. When studied after discharge from the hospital, the patient rested quietly in bed from one-half to one hour before measurements were made. Serum cholesterol measurements were made in duplicate by the method of Myers and Wardell[29] using the continuous extraction apparatus described by Ling.[22] Blood was drawn from the antecubital vein with minimal stasis, after a fast of fourteen hours or more. The arm-to-tongue circulation time, as measured by the decholin method of Winternitz, Deutsch and Brull[40] was used as an index of the velocity of blood flow. The heart rates were measured in the basal state. Blood pressure measurements were made by means of a standard mercury manometer with a cuff 14 cm. wide. The readings represent the mean values of repeated measurements made with the patient at rest. The above measurements and clinical observations at various time intervals were obtained on the same day or subsequent days.

FACTORS EMPLOYED IN GAUGING THE DEGREE OF HYPOTHYROIDISM

Although measurement of the basal metabolism is the most useful single estimation available for evaluating the degree of thyroid activity, the basal metabolic determinations fail at times to conform to those ex-

*All operations were performed by Dr. David D. Berlin.

pected from clinical studies. For example, no clinical evidence of reduced thyroid activity may be manifest in certain patients whose basal metabolic rates are reduced as low as 25 or even 35 per cent below the average normal.[27] On the other hand, the administration of dinitro-orthocresol or dinitrophenol[13, 36] to patients with myxedema may increase the metabolic rate, with little or no influence on the clinical signs and symptoms of myxedema. The rise in metabolic rate after the administration of dinitrophenol or dinitro-orthocresol to normal persons or to patients with myxedema is not accompanied by the nervous symptoms and cardiovascular manifestations which are subsequent to thyroid administration.[13, 36] In the light of these facts, the metabolic rate must be considered merely one expression of the underlying hypothyroid state.

The importance of the serum cholesterol value as an aid in estimating the degree of spontaneous myxedema has been stressed by Hurxthal,[19, 20, 23] and the findings in artificial myxedema will be described by us in a forthcoming communication.[17] In some patients the height of the serum cholesterol was in closer agreement with the clinical signs and symptoms of hypothyroidism than the basal metabolic rate (Cases 5, 12, 15, 16).

The relation between the metabolic rate and velocity of blood flow in health and disease has been described in previous communications.[5, 6, 7, 38] In patients with cardiovascular disease and a normal metabolic rate, the velocity of blood flow is slowed according to the degree of circulatory insufficiency. The blood flow may be similarly slowed in patients with no cardiac failure but with the low metabolic rates of myxedema. The velocity of blood flow in the latter patients is a further index of the degree of hypothyroidism.

The development of clinical signs and symptoms of hypothyroidism following operation usually indicated roughly the degree of the hypothyroid state. As the basal metabolic rate became significantly lowered following operation, mild signs and symptoms, such as dryness of the skin, slow growth of hair, slight hoarseness, and coldness of the extremities, appeared. The interval between operation and the development of these signs and symptoms and of a markedly reduced basal metabolic rate varied usually from three weeks to two months. These early symptoms caused little or no discomfort and did not require thyroid medication. As the basal metabolic level continued at or below approximately minus 30 per cent, many patients showed weakness of the legs, puffiness of the face and hands, drowsiness, and irritability. These "untoward symptoms" of myxedema were controlled by means of small doses of thyroid (Armour's), one-eighth to one-half grains daily.

TABLE I

RELATIONSHIP OF BASAL METABOLIC RATE, VELOCITY OF BLOOD FLOW AND BLOOD CHOLESTEROL TO CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM OF THE HEART IN PATIENTS WITH CONGESTIVE FAILURE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS. CARDIAC DIAM. CM.	LENGTH CM.	BASE CM.	HALF CHEST DIAM. CM.	B. M. R. PER CENT	VBF IN SECONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
1.	*L. B.*	F	44	Pre-op.	13.9	14.2	11.2	11.0	− 9	20	132		60	140/78
	R. H. D.			1 mo.	13.6	14.1	11.0	11.1	−32	23			44	112/82
				2½ mo.	13.9	14.8	11.3	10.9	−25		310		60	140/90
				6 mo.	15.4	15.8	11.0	11.1	−37		385		58	130/86
				8½ mo.	16.6	16.7	12.3	11.1	−32		400		70	128/76
2.	*H. G.*	M	22	Pre-op.	15.3	17.0	12.7	14.5	+ 7	34	138		80	110/60
	R. H. D.			1½ mo.	16.9	17.9	14.0	14.9	−28	42			70	118/70
				3½ mo.	17.2	18.1	14.2	14.8	−27	56	251		88	
				4½ mo.	17.7	17.7	14.4	14.9	−22	51		0.4 mg. thyroxin daily	70	116/80
				5 mo.	16.9	17.3	12.8	14.4	−38	37	236		66	110/68
3.	*E. W.*	M	27	Pre-op.	17.3	17.3	13.4	15.9	+ 5	23	127		80	110/60
	R. H. D.			1 mo.	18.0	17.5	14.9	16.1	−22	40	135		76	104/60
				3 mo.	18.9	18.2	13.3	16.2	−27	52	149		80	110/66
				6½ mo.	19.6	19.4	13.3	16.4	−34	43	181		70	106/66
4.	*C. C.*	M	66	Pre-op.	15.8	18.5	13.0	14.8	+ 9	33	154		47	130/70
	H. H. D.			3 wk.	16.3	18.0	11.8	14.8	−23	66	147		45	116/68
	L. H. D.			1 mo.	18.0	19.3	11.2	14.5	−36	50	207		50	112/68
				1½ mo.	16.8	19.2	12.7	15.0	−23	40	196	gr. ⅓ daily	65	128/70
				6½ mo.	16.7	18.2	13.2	15.0	−30	53	206	gr. ⅕ daily	58	110/70
5.	*S. Br.*	F	47	Pre-op.	17.8	18.0	11.7	13.4	+13	24	161		72	198/110
	R. H. D.			3½ mo.	19.7	20.0	14.5	13.6	− 4	81	364		56	148/90

R. H. D.—Rheumatic heart disease
A. H. D.—Arteriosclerotic heart disease
H. H. D.—Hypertensive heart disease
L. H. D.—Luetic heart disease
A. P.—Angina pectoris
C. A.—Cardiac asthma
C. T.—Healed coronary thrombosis
B. A.—Bronchial asthma
C. P.—Cor pulmonale

TABLE I—CONT'D

6.	*F. C.*	M	35	Pre-op.	15.1			13.6	− 4	22	154		66	118/80
	B. A.			1 mo.	15.6			13.5	−24	32	217		50	112/86
	C. P.			2 mo.	14.9			13.6	−32	31			56	112/86
				4½ mo.	15.9	17.0	11.0	13.5	−27	28	255		66	112/90
				6 mo.	15.8	17.0	12.3	13.6	−26	39			76	116/92
				8 mo.	17.0	18.7	13.5	13.7	−37	38	216	gr. ⅕ daily	70	108/92
7.	*F. Z.*	M	19	Pre-op.	17.0	19.1	13.9	13.6	+ 1	26	138		90	300/ 0
	R. H. D.			3½ mo.	18.6	20.2	14.5	13.8	−10	25	254		98	200/ 0
	C. A.													
8.	*S. Be.*	F	51	Pre-op.					+ 4	31	154		70	140/82
	R. H. D.			1 mo.	14.6	16.5	13.6	12.9	−12		311		82	132/88
				3 mo.	16.0	16.6	12.5	12.9	−17	40	128		62	112/60
				4 mo.	16.2	16.8	13.5	12.8	−14	55	246	gr. ¼ daily	60	120/60
				5 mo.	15.5	14.8	11.8	12.7	+ 8		182		60	132/82
				6 mo.	15.8	16.6	11.9	12.3	+ 4	38			76	120/80
9.	*H. G.*	F	38	Pre-op.	14.6	14.8	8.7	11.8	− 8	29			41	220/98
	H. H. D.			2 mo.	16.0	15.4	9.8	11.6	−25	38	292		56	200/98
				3 mo.					−36	42	345	gr. 1 for 5 days	45	186/100
10.	*W. B.*	M	55	Pre-op.	13.6			12.4	+ 9	18	294		66	180/110
	H. H. D.			3 wk.	14.6	18.4	16.3	12.9	−15	23	335		70	128/80
	C. A.			1½ mo.	14.8			12.8	−24	24	388		56	140/82
	A. P.			6½ mo.	14.3			13.3	−33	34	410	gr. ⅓ daily—1 mo.	62	155/90
11.	*G. F.*	M	52	Pre-op.	17.4			14.8	− 1	45			70	130/80
	A. P.			1 mo.	18.2			14.6	−23	48			50	102/70
	R. H. D.			5 mo.	18.0			14.7	−25	41			58	
	C. T.			7 mo.	17.9			14.6	−26				60	
				10 mo.	18.5			14.5	−25	40			70	
				12 mo.	17.7			14.6	−26				63	

TABLE I—CONT'D

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS. CARDIAC DIAM. CM.	LENGTH CM.	BASE CM.	HALF CHEST DIAM. CM.	B. M. R. PER CENT	VBF IN SECONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
12.	*J. R.*	M	63	Pre-op.	17.0	17.4	9.4	12.6	+24	52			70	122/86
	A. H. D.			2 mo.	17.8	17.4	9.7	12.8	–22	80	328		66	106/82
				2½ mo.	17.9	18.0	11.1	13.3	–17	90	424		68	126/82
				3½ mo.	16.4	17.0	11.0	13.7	–18			gr. ⅛ daily		
13.	*F. D.*	M	18	Pre-op.	15.9	17.0	12.9	13.6	–12	31	172		80	120/66
	R. H. D.			3½ mo.	16.7	17.4	11.6	13.9	–36	34	323		80	120/80
14.	*W. D.*	M	22	Pre-op.	17.7			15.0	– 8	51	92		65	132/90
	R. H. D.			1 mo.	17.0			14.6	–32	57	140		72	120/76
				3 mo.	17.2			15.1	–27	41	152		80	110/62
				5 mo.	18.4			14.8	–24	48	283		72	130/88
				8 mo.	16.9			14.7	–19	35	170	gr. ⅕ daily		
				9 mo.	16.5	17.0	13.4	14.7	–26	66	204	gr. ⅛ daily	66	130/88
15.	*B. Z.*	F	45	Pre-op.	17.3	18.3	13.7	13.2	– 5	30	167		50	150/62
	R. H. D.			1 mo.	17.3	17.2	13.2	13.8	–30	31	214		45	120/72
				3 mo.	18.0	17.6	12.3	13.4	–27				56	112/78
				6 mo.	17.6			13.3	–20	53	408		54	118/60
				8 mo.	17.6	17.6	13.6	13.5	–21	38	448		60	
16.	*B. C.*	F	35	Pre-op.	14.6	15.0	12.6	12.7	– 1	23	145		76	108/80
	R. H. D.			1 mo.	14.5	16.4	12.1	12.8	–33	25	280		76	110/80
				2 mo.	13.4	13.7	10.8	13.1	–19	32	317		60	112/90
				3½ mo.	14.5	14.2	11.2	13.2	–27	26			74	

TABLE I—CONT'D

17.	*W. B.* A. P. A. H. D.	M	63	Pre-op. 3 mo.	14.7 14.5	16.0 17.7	10.9 9.2	15.0 15.3	–10 –41	18 23	117 428		65 52	122/76
18.	*L. M.* R. H. D.	M		Pre-op. 1 mo. 3 mo. 5 mo.	18.1 17.6 17.8 17.8	19.7 18.8 19.2 18.5	13.6 12.8 11.6 13.7	15.8 15.8 15.9 16.0	+ 6 –34 –30 –26	42 42 42 38	135 345 400		84 66 78 70	110/56 110/80 130/95 134/86
19.	*E. M.* H. H. D.	F	50	Pre-op. 2 mo.	18.6 18.0	18.4 17.4	11.2 11.0	14.8 14.7	– 4 –23	21 22	366		78 64	168/98
20.	*B. R.* R. H. D.	F	48	Pre-op. 1½ mo.	19.3 18.2	19.5 18.4	14.7 12.3	13.8 14.1	+ 3 –14	33 30	404		72 92	172/110 148/80
21.	*J. T.* H. H. D.	M	59	Pre-op. 5½ mo.	17.3 16.0	18.0 16.0	13.2 12.3	14.1 14.2	– 3 –20	57 29	330		58 65	140/80 148/86
22.	*E. D.* R. H. D. C. A.	M	22	Pre-op. 3 wk. 1 mo. 2½ mo. 3½ mo.	26.5 25.0 25.1 23.2 24.3	23.1 23.6 24.7 23.5 21.9	17.9 15.8 16.0 15.2 15.3	15.8 16.0 16.0 15.8 16.2	– 3 –30 –37 –32 –27	43 48 71 66 32	109 203	gr. ⅓ daily	55 50 52 52 48	140/70 106/62 132/70 110/78 118/72

CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM

The relationship of the degree of hypothyroidism to the changes in the seven-foot roentgenogram is summarized in Table I. Cases are arranged in the order of decreasing changes in cardiac transverse diameter. The first group comprised twenty-two patients with congestive failure due to various types of heart disease (Table I). The heart size and electrocardiograms, preoperatively, showed varying deviations from the normal. In twenty of these cases the transverse cardiac diameter was greater than one-half the internal chest diameter. Following thyroidectomy, the transverse cardiac diameter increased more than 0.5 cm. in fifteen patients, showed no change in three patients and decreased more than 0.5 cm. in four patients. The greatest increase in size was

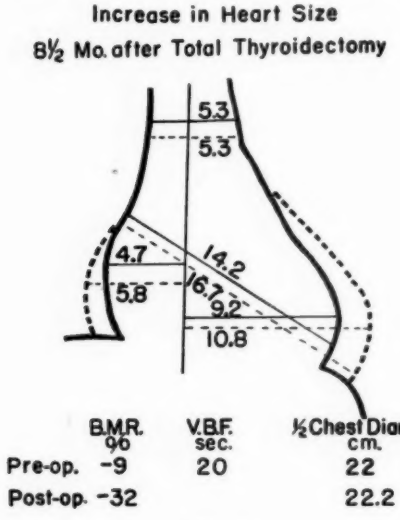

Fig. 1.

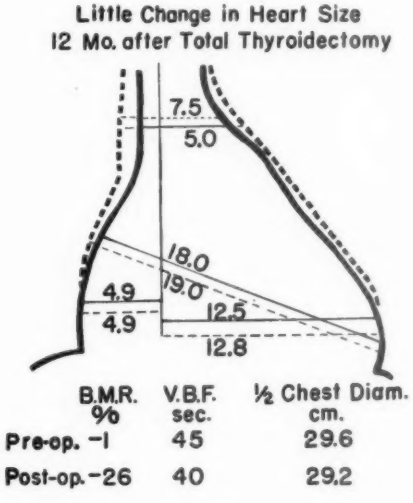

Fig. 2.

Fig. 1.—Silhouettes of heart before and after operation in Case 1. Black line represents preoperative cardiac outline; dotted line, silhouette twelve months after operation.

Fig. 2.—Silhouettes of heart before and after operation in Case 11. Black line represents pre-operative cardiac outline; dotted line, silhouette twelve months after operation.

2.7 cm.; the greatest decrease in size was 1.4 cm. The changes in heart size observed in the group with congestive failure were the resultant of two opposing tendencies: the increase in cardiac size that takes place in myxedema, and the shrinkage in heart size that accompanies the return to compensation of a heart previously decompensated. This shrinkage varied with the degree of dilatation previously present because of heart failure. According to whether one tendency or the other predominated, the heart size of the different patients in this group with congestive failure decreased, increased, or showed little or no change. (Figs. 1, 2, and 3.)

The second group comprised ten patients with angina pectoris and one patient with angina pectoris produced by paroxysmal auricular

fibrillation (Table II). In five cases the transverse cardiac diameters, preoperatively, were greater than one-half the internal chest diameters. After operation eight patients showed an increase of 0.5 cm. or more in the transverse cardiac diameter, coincident with the drop in metabolism, and three showed no change.

The third group comprised patients with no heart disease (Table III). Three of the four patients showed an increase in the transverse cardiac diameter, the greatest increase being 2.8 cm. (Case 34).

THE RELATION OF CHANGES IN HEART SIZE TO CHANGES IN THE BASAL METABOLIC RATE

The basal metabolic rate gradually decreased after total thyroidectomy, the maximum decrease occurring usually between the third and

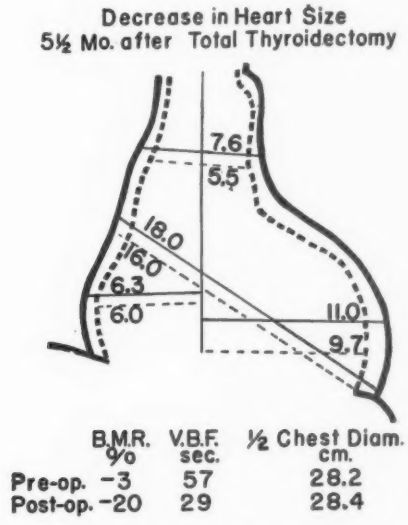

Fig. 3.—Silhouettes of heart before and after operation in Case 21. Black line represents preoperative cardiac outline; dotted line, silhouette five and one-half months after operation.

the eighth week. An increase in heart size was observed as early as the third week after operation, at which time the metabolic rate had not yet reached its lowest level (Cases 4 and 26). The increases in heart size following thyroidectomy usually developed coincident with the gradual lowering of the basal metabolic rate. Changes in measurements of the length and base of the heart usually corresponded with changes in the transverse cardiac diameter. Case 3 showed an increase of 0.7 cm. as the basal metabolic rate dropped from plus 5 to minus 22 per cent. With a further drop to minus 27, and later to minus 34 per cent, the cardiac diameter showed progressive increases of 1.6 and 2.3 cm. respectively over the preoperative values. In Case 10 there was an increase of 1 cm. as the basal metabolic rate dropped from plus 9 to

TABLE II

RELATIONSHIP OF BASAL METABOLIC RATE, VELOCITY OF BLOOD FLOW AND BLOOD CHOLESTEROL TO CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM OF THE HEART IN PATIENTS WITH ANGINA PECTORIS BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS. CARDIAC DIAM. CM.	LENGTH CM.	BASE CM.	HALF CHEST DIAM. CM.	B. M. R. PER CENT	VBF IN SECONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
23.	*M. G.*	F	37	Pre-op.	19.5	20.3		13.5	+ 3	18			80	110/60
	R. H. D.			1½ mo.	22.5	21.0		13.5	–11	27	311		60	
	A. P.													
24.	*S. F.*	M	52	Pre-op.	17.3	18.4	10.4	15.5		23			76	
	A. P.			1½ mo.	17.6	18.2	11.3	15.5	–20		234		66	
	Cor.			2 mo.	19.6	18.2	11.3	15.5		19		gr. ¼ daily		
25.	*A. B.*	M	59	Pre-op.	11.2			14.5	– 8	24	211		63	140/80
	A. P.			1½ mo.	12.9			14.7	–18	18			69	132/78
				3 mo.	13.3			14.3	–30	21	298		58	138/80
				6½ mo.	12.9			14.4	–31	25	315	gr. ⅓ daily	72	140/60
				9½ mo.	13.1	14.9	12.0	14.4	+12	22		gr. ⅕ daily	64	138/80
26.	*M. H.*	M	54	Pre-op.	16.2	17.5	11.3	15.6	+ 5	20			70	180/110
	A. P.			½ mo.	18.1	17.6	10.7	16.0	– 5	20	333		60	152/92
27.	*M. W.*	M	54	Pre-op.	10.4	15.2	10.4	14.3	– 8	19	119		72	118/76
	A. P.			1½ mo.	11.8	14.8	7.9	14.7	–18	23	284		75	130/60
	Cor.			5½ mo.	11.9	15.4	10.4	14.7	–34	34	262		70	120/80

R. H. D.—Rheumatic heart disease
H. H. D.—Hypertensive heart disease
A. H. D.—Arteriosclerotic heart disease
A. P.—Angina pectoris
B. A.—Bronchial asthma
Cor.—Healed coronary thrombosis

TABLE II—CONT'D

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS. CARDIAC DIAM. CM.	LENGTH CM.	BASE CM.	HALF CHEST DIAM. CM.	B.M.R. PER CENT	VBF IN SECONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
28.	*G. O.*	M	65	Pre-op.	13.4	15.6	10.2	15.5	–13	15	154		68	136/76
	A. P.			1½ mo.	15.6	17.6	9.9	15.5	–28	31	322		80	136/80
	B. A.			5½ mo.	14.9	16.8	10.0	15.0	–30	21	280		66	130/84
29.	*R. S.*	F	57	Pre-op.	11.3	13.5	9.3	13.4	+ 3	16	292		88	210/72
	A. P.			3½ mo.	12.2	13.7	9.5	13.7	–16	21	555		64	166/80
				4 mo.	12.3	13.2	9.7	13.2	– 4	24			66	138/88
30.	*M. C.*	M	57	Pre-op.	13.4	13.8	10.3	15.0	–24	16	192		70	140/82
	A. P.			1½ mo.	14.0	15.8		14.4	–34	18	347		80	136/80
31.	*M. V.*	F	59	Pre-op.	13.6			13.0	–12		231		80	172/66
	A. P.			1 mo.	13.6	14.7	9.0	13.4	–22				72	122/88
	A. H. D.			3 mo.	13.9	14.6	9.1	12.9	–31				78	130/88
	H. H. D.			6 mo.	13.5	14.9	8.9	13.2	–26		343		68	140/90
32.	*E. P.*	F	59	Pre-op.	13.4	13.8	8.1	12.7	–23	19	298		60	146/80
	A. P.			1½ mo.	13.4	14.0	9.8	13.1	–27	25	482		72	138/90
	A. H. D.			5 mo.	14.0	15.0	9.1	12.9	–33		479	gr. ¼ daily	60	146/90
	H. H. D.													
33.	*M. F.*	M	48	Pre-op.					–14	18			60	140/96
	A. P.			1 mo.	15.3	16.2	11.1	15.9	–16	17			64	140/60
	Cor.			5½ mo.	15.1	16.5	11.9	15.7	–33	31	450		88	

TABLE III

RELATIONSHIP OF BASAL METABOLIC RATE, VELOCITY OF BLOOD FLOW AND BLOOD CHOLESTEROL TO CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM OF THE HEART IN PATIENTS WITHOUT HEART DISEASE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS. CARDIAC DIAM. CM.	LENGTH CM.	BASE CM.	HALF CHEST DIAM. CM.	B. M. R. PER CENT	VBF IN SECONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
34.	*W. Mc.*	M	63	Pre-op.	8.7			13.8	+ 1	15	168		84	
				1 mo.	11.1	14.1	9.3	13.6	–21	20	320		76	
				3 mo.	11.5	13.6	10.3	13.8	–31	20	305		84	
				5½ mo.	10.2	14.0	10.0	13.8	–10	23			72	120/80
				8 mo.	11.5			14.0		19	301	gr. 1 t.i.d. for 7d.		
35.	*F. F.*	M	52	Pre-op.	13.4	16.8	10.1	14.8	0	22			68	
				3 wk.	13.1	15.9	13.1	15.0	–13	17			70	
				2½ mo.	14.7			15.2	–25	31			70	
36.	*M. A.*	F	19	Pre-op.	7.8	12.0	8.6	11.0	– 7	14			88	110/66
				2 mo.	8.7	12.2	9.2	11.6	–41		400		72	90/60
				3½ mo.	8.8	13.0	9.1	11.4	0	13	269	gr. ¼ daily	84	110/90
37.	*M. D.*	F	24	Pre-op.	11.0			14.7	+10	9			80	
				2 mo.	10.9	13.0	12.2	12.8	–32	14			78	110/68
									–34	17		gr. ¼ daily		

minus 15 per cent. In Case 11 the basal metabolism remained exceptionally constant from the first to the twelfth month after operation. During this time the transverse diameter showed no marked changes, although with the initial lowering in metabolic rate during the first postoperative month the heart size had increased appreciably. The administration of small doses of thyroid, as indicated in Tables I, II, and III, caused a prompt decrease in heart size in some patients.

In patients with congestive failure increased heart size did not always parallel lowering in the metabolic rate. With clinical improvement, and consequently lessened cardiac dilatation, the heart sometimes became smaller. In patients with angina pectoris, however, and in those patients with congestive failure who had reached the stage of compensation, changes in the metabolic rate were usually accompanied by corresponding changes in heart size (Table I). In Case 4 the basal metabolic rate had dropped from plus 9 to minus 36 per cent by the end of the fourth postoperative week, and the transverse cardiac diameter had increased 2.2 cm. Two weeks later, after thyroid medication, the basal metabolic rate had increased to minus 23 per cent, and the transverse cardiac diameter had shrunk 1.2 cm. below its one month diameter. Similar responses were seen in Cases 14 and 8.

In some instances (Cases 5, 7, and 29) the basal metabolic rate was not markedly lowered in patients who showed definite clinical manifestations of hypothyroidism. In these cases the changes in heart size corresponded to the degree of hypothyroidism as indicated by the elevated serum cholesterol values and by the clinical findings.

RELATION OF CHANGES IN ELECTROCARDIOGRAMS TO THE DEVELOPMENT OF THE HYPOTHYROID STATE

The electrocardiographic changes following total thyroidectomy have been observed in thirty-two patients (Tables IV, V, VI). The case numbers correspond with those of Tables I, II, and III. The voltages of the R- and T-waves in all three leads are recorded. The T-wave measurements represent the greatest voltage above and below the base line. The electrical axis was calculated according to the method of Einthoven and showed no significant variations. Changes in the voltage of T-waves in some cases are partly attributable to varying degrees of digitalization and of coronary and myocardial disease. Minor variations in the P-R and QRS intervals in a few instances may be related to the same factors. Definite diminution in the amplitude of the ventricular complexes which could not be attributed to the above factors was evident in twenty-four of the thirty-two patients studied. In these patients diminution in amplitude generally appeared with the first significant drop in the metabolic rate (Cases 1, 3, and 4). The greatest change occurred with the maximum development of hypothyroidism. In these cases the P-R and QRS interval usually showed no change after operation.

TABLE IV

RELATIONSHIP OF BASAL METABOLIC RATE TO CHANGES IN THE ELECTROCARDIOGRAM IN PATIENTS WITH CONGESTIVE FAILURE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE	RATE PER MIN.	P-R INT. SEC.	QRS INT.	VOLTAGE IN MILLIVOLTS						B. M. R. PER CENT	TIME INTERVAL
							R_1	R_2	R_3	T_1	T_2	T_3		
1.	L. B.	F	44	60	A. F.*	0.06	0.50	1.30	1.10	0.20	0.20		− 9	Pre-op.
				60	A. F.	0.06	0.30	0.70	0.70	0.05	0.10		−32	2 weeks
				80	A. F.	0.06		0.60			0.20		−25	2½ months
				70	A. F.	0.04	0.10	0.40	0.60	0.00	0.00	0.00	−37	6 months
				70	A. F.	0.04	0.10	0.50	0.60	0.00	0.00	0.00	−32	8 months
2.	H. G.	M	22	100	A. F.	0.08	0.50	1.20	0.90	−0.15	−0.10		+ 7	2 weeks
				120	A. F.	0.08	0.20	0.60	0.40	−0.05	0.10	0.00	−28	1½ month
				130	A. F.	0.08	0.30	0.60	0.60	−0.05	−0.07		−27	3 months
3.	E. W.	M	27	85	0.22	0.08	0.30	1.00	1.30	0.20	0.20	−0.10	+ 5	Pre-op.
				85	0.20	0.06	0.20	0.70	0.90	0.15	0.15	±0.10		2 weeks
					0.22	0.08	0.20	0.70	0.90	0.10	0.15	±0.05	−22	1½ months
					0.22	0.08	0.30	0.80	1.10	0.10	0.15	0.00	−27	3 months
					0.21	0.08	0.30	0.50	0.70	0.05	0.13	0.10	−34	6 months
4.	C. C.	M	66	80	0.20	0.11	1.20	0.75	0.40	−0.15	0.00	0.20	+ 9	Pre-op.
				60	0.20	0.12	1.10	0.50	0.20	−0.20	−0.03	0.20	−23	2 weeks
				60	0.16	0.12	1.20	0.35	0.20	−0.10	0.00	0.10	−36	1 month
				65	0.20	0.12	1.10	0.60	0.30	−0.15	0.00	0.20	−23	2 months
				70	0.20	0.12	0.80	0.50	0.20	−0.10	0.03	0.15	−30	7 months
5.	*S. Br.*	F	47	80	A. F.		0.40	0.60	0.60	±0.05	±0.07	+0.05	+13	Pre-op.
				60	A. F.		0.50	0.50	0.40	±0.06	±0.06	+0.05	− 4	2 weeks
				80	A. F.	0.08	0.40	0.20		0.10	0.00			3 months
6.	F. C.	M	35	105	0.16	0.08	0.45	0.80	1.40	0.20	−0.20	−0.20	− 4	Pre-op.
				55	0.16	0.08	0.50	0.70	1.10	0.10	−0.15	−0.20	−24	2 weeks
				80	0.19	0.08	0.40	0.55	0.90	0.15	−0.19	−0.15	−32	2½ weeks
				70	0.18	0.08	0.40	0.50	0.80	0.03	−0.15	−0.15	−27	1 month
				80	0.18	0.07	0.00	0.60	1.00	0.10	±0.05	−0.15	−26	6 months
				90	0.18	0.06	0.20	0.70	1.90	0.20	−0.10	−0.15	−37	8 months
				80	0.19	0.07	0.15	0.60	1.20	0.10	−0.05	−0.15	−22	10 months

TABLE IV—CONT'D

NO.	INIT.	SEX	AGE	RATE PER MIN.	P-R INT. SEC.	QRS INT.	VOLTAGE IN MILLIVOLTS						B. M. R. PER CENT	TIME INTERVAL
							R_1	R_2	R_3	T_1	T_2	T_3		
7.	F. Z.	M	19	80	0.24	0.11	1.20	0.70	0.50	±0.10	±0.20	0.15	+ 1	Pre-op.
				80	0.26	0.12	2.20	1.30	0.90	±0.20	±0.20	0.20		2 weeks
					0.24	0.13	1.50	0.60	0.50	−0.30	0.40	0.50	−10	3½ months
8.	S. Be.	F	51	110	A. F.	0.04	0.40	1.50	1.10	0.10	−0.15	−0.15	+ 4	Pre-op.
				85	A. F.	0.04	0.20	0.80	0.70	0.10	−0.15	−0.15	−12	1 month
				80	A. F.	0.04	0.30	1.00	0.90	0.00	−0.15	−0.15	−23	3 months
				90	A. F.	0.06	0.20	0.70	0.60	0.05	−0.05	−0.07	−14	4 months
10.	W. B.	M	55	80	0.16	0.07	1.30	1.50	0.35	−0.05	−0.20	−0.15	+ 9	Pre-op.
				70	0.14	0.07	1.00	1.40	0.35	0.00	−0.17	−0.10	−15	1 month
				60	0.16	0.07	1.20	1.20	0.30	0.00	−0.18	−0.10	−24	2 months
				75	0.16	0.06	1.00	1.20	0.30	−0.05	−0.15	−0.15	−33	7 months
11.	G. F.	M	52	80	A. F.	0.08	0.70	0.90	0.40	0.25	0.25	0.00	− 1	Pre-op.
				50	A. F.	0.06	0.90	0.80	0.30	0.15	0.15	−0.10	−23	2 months
				65	A. F.	0.06	0.80	0.70	0.30	0.10	0.15	−0.05	−25	5 months
				60	A. F.	0.07	0.60	0.50	0.20	0.05	0.00	0.00	−25	10 months
				90	A. F.	0.06	0.60	0.60	0.20	0.00	0.05	0.00	−26	12 months
12.	J. R.	M	63	80	A. F.	0.08	1.50	0.20	0.00	−0.20	0.00	0.20	+24	Pre-op.
				70	A. F.	0.08	1.60	0.00	0.00	−0.15	0.10	0.20	−22	2 months
				80	A. F.	0.07	0.80	0.00	0.00	±0.06	0.05	0.10	−18	3 months
13.	F. D.	M	18	95	A. F.	0.05	0.20	0.80	0.80	0.10	−0.15	−0.10	−12	Pre-op.
				80	A. F.	0.08	0.30	0.80	0.90	−0.10	±0.10		−36	4 months
				100	A. F.	0.08	0.30	0.90	1.00	0.10				5 months
14.	W. D.	M	22	75	0.22	0.08	0.30	0.65	0.80	0.15	0.20	±0.05	− 8	Pre-op.
				75	0.21	0.08	0.15	0.75	0.60	0.05	0.10	0.00	−32	1 week
				60	0.25	0.07	0.20	0.75	0.55	0.00	±0.10	±0.05	−27	1 month
				65	0.20	0.08	0.10	0.90	0.70	±0.05	±0.10	±0.05	−19	9 months

TABLE IV—CONT'D

NO.	INIT.	SEX	AGE	RATE PER MIN.	P-R INT. SEC.	QRS INT.	VOLTAGE IN MILLIVOLTS						B. M. R. PER CENT	TIME INTERVAL
							R_1	R_2	R_3	T_1	T_2	T_3		
15.	B. Z.	F	45	70	A. F.	0.08	0.30	1.00	1.30	±0.05	−0.20	−0.10	− 5	Pre-op.
				59	A. F.	0.08	0.10	0.70	0.80	0.00	−0.15	−0.10	−30	1 month
				55	A. F.	0.08	0.10	0.60	0.80	−0.05	−0.15	−0.05		1½ months
				65	A. F.	0.08	0.10	0.50	0.70	−0.00	−0.10	0.00	−20	6 months
				60	A. F.	0.06	0.10	0.50	0.70	−0.10	−0.15	−0.05	−21	8 months
16.	B. C.	F	35	70	A. F.	0.06	0.30	0.80	0.50	0.10	0.15	0.15	− 1	Pre-op.
				120	A. F.	0.06	0.40	0.60	0.40				−33	1 month
				70	A. F.	0.06	0.40	0.70	0.40				−19	2 months
				70	A. F.	0.08	0.40	0.60	0.30				−27	4 months
17.	W. B.	M	63	65	0.16	0.04	0.08	0.40	0.00	0.15	0.13	0.00	−10	Pre-op.
				75	0.17	0.06	0.40	0.20	0.00	−0.10	−0.15	0.00	−41	3 months
18.	L. M.	M	55	90	0.20	0.12	0.40	0.10	0.00	±0.05	0.00	0.05	+ 6	Pre-op.
				70	0.20	0.12	0.30	0.00	0.00	−0.10	0.00	0.00		2 weeks
				90	0.20	0.12	0.50	0.00	0.00	0.00	0.00	0.10	−30	3 months
				90	0.18	0.12	0.40	0.00	0.00	0.00	0.07	0.05	−26	5 months
20.	B. R.	F	48	85	A. F.	0.06	1.00	1.00	0.10	0.10	0.15	0.13	+ 3	Pre-op.
				70	A. F.	0.06	1.10	1.00	0.10	−0.15	0.00	0.10	−14	2 months
21.	J. T.	M	59	120	A. F.	0.12	0.60	0.00	0.00	−0.10	0.20	0.30	− 3	Pre-op.
				90	A. F.	0.12	1.10	0.00	0.00	−0.20	0.25	0.40	−28	2 months
				65	A. F.	0.08	0.50	0.00	0.00	−0.05	0.10	0.15	−20	6 months
22.	R. D.	M	22	90	A. F.	0.08	0.80	1.50	1.00	−0.10	0.15	0.15	− 3	Pre-op.
				70	A. F.	0.08	0.60	1.00	0.90	±0.05	0.20	0.10	−30	3 weeks
				70	A. F.	0.08	0.60	0.95	0.70	±0.05	0.15	0.20	−32	2 months
				70	A. F.	0.08	0.60	1.00	0.70	−0.10	0.06	0.10	−27	4 months

*A. F.—Auricular fibrillation.

TABLE V

RELATIONSHIP OF BASAL METABOLIC RATE TO CHANGES IN THE ELECTROCARDIOGRAM IN PATIENTS WITH ANGINA PECTORIS BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE YEARS	RATE MIN.	P-R INT. SEC.	QRS INT. SEC.	VOLTAGE IN MILLIVOLTS						B. M. R. PER CENT	TIME INTERVAL
							R_1	R_2	R_3	T_1	T_2	T_3		
25.	A. B.	M	59		0.17	0.08	0.70	1.20	0.60	0.10	0.25	0.00	– 8	Pre-op.
				85	0.18	0.08	0.50	1.10	0.60	0.00	0.15	0.05		2 weeks
				90	0.17	0.09	0.40	0.90	0.50	0.00	0.05	0.00	–18	2 months
				80	0.18	0.09	0.50	0.90	0.60	0.07	0.10	0.10		8 months
26.	H. K.	M	58	75	0.20	0.11	0.60	0.90	0.80	0.10	0.15	0.10	–17	Pre-op.
				60	0.20	0.12	0.60	0.60	0.30	0.05	0.10	0.03	–29	2 weeks
27.	M. W.	M	54	80	0.20	0.06	0.35	0.10	0.10	±0.05	0.05	0.10	– 7	Pre-op.
				90	0.18	0.08	0.30	0.20	0.20	0.00	0.03	0.00	–18	2 weeks
				75	0.16	0.08	0.40	0.10	0.10	0.05	0.00	0.00	–19	3 months
					0.16	0.06	0.35	0.10	0.10	0.03	0.05	0.05	–34	5 months
28.	G. O.	M	65	70	0.22	0.06	0.40	0.20	0.00	0.00	0.10	0.10	–13	Pre-op.
				80	0.20	0.04	0.20	0.30	0.00	0.00	0.10	0.10	–28	1 month
				85	0.21	0.06	0.40	0.30	0.00	0.00	0.00	0.05	–30	4 months

TABLE V—CONT'D

NO.	INIT.	SEX	AGE YEARS	RATE MIN.	P-R INT. SEC.	QRS INT. SEC.	VOLTAGE IN MILLIVOLTS						B. M. R. PER CENT	TIME INTERVAL
							R_1	R_2	R_3	T_1	T_2	T_3		
30.	M. C.	M	57	85	0.20	0.06	0.60	0.60	0.00	±0.05	0.05	0.00	–24	Pre-op.
				100	0.20	0.06	0.60	0.40	0.00	±0.10	–0.10	–0.05	–26	2 weeks
				100	0.16	0.06	0.40	0.20	0.00	0.05	0.05	0.00	–32	2 months
				100	0.16	0.06	0.40	0.60	0.00	0.05	0.10	0.00	–32	5 months
31.	M. V.	F	59	65	0.16	0.08	2.00	1.50	0.80	0.15	0.15	–0.13	–12	Pre-op.
				90	0.16	0.07	1.40	1.20	0.50	±0.10	0.05	0.00	–22	1 month
				85	0.16	0.07	1.10	1.70	0.50	±0.15	0.08	0.10	–31	3 months
32.	E. P.	F	58	60	0.18	0.08	0.90	0.30	0.25	0.20	0.25	0.00	–23	Pre-op.
				85	0.20	0.06	0.80	0.00	0.20	0.10	0.10	0.00	–27	1 month
				85	0.18	0.06	0.60	0.15	0.15	0.15	0.10	0.00		2 months
				70	0.18	0.08	0.50	0.10	0.20	0.10	0.15	0.10	–33	5 months
33.	M. F.	M	48	70	0.16	0.06	1.50	0.90	0.10	–0.20	–0.10	0.10	–14	Pre-op.
				80	0.16	0.06	1.20	0.50	0.00	0.05	0.00	0.00	–16	1 month
				60	0.16	0.06		1.10			–0.10		–27	4 months
				70	0.16	0.08	1.10	0.80	0.00	0.03	0.03	0.00	–33	5 months
				75	0.14	0.06	0.70	0.40	0.00	0.00	0.00	0.00	–36	6½ months

TABLE VI

RELATIONSHIP OF BASAL METABOLIC RATE TO CHANGES IN THE ELECTROCARDIOGRAM IN PATIENTS WITHOUT HEART DISEASE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE YEARS	RATE MIN.	P-R INT. SEC.	QRS INT. SEC.	VOLTAGE IN MILLIVOLTS						B. M. R. PER CENT	TIME INTERVAL
							R_1	R_2	R_3	T_1	T_2	T_3		
36.	W. M.	M	63	105	0.16	0.08		0.80			0.25		+ 1	Pre-op.
				65	0.20	0.07		0.40			0.00		−31	3 months
				80	0.16	0.08	0.30	0.60	0.40	0.00	0.20	0.10	−10	6 months
				70	0.16	0.06	0.40	0.40	0.20	0.00	0.00	0.00		8 months
37.	F. F.	M	52	100	0.20	0.06		0.40			0.10		0	Pre-op.
				70	0.21	0.06		0.50			0.10		−13	3 weeks
				75	0.20	0.07		0.20			0.00		−25	3 months
38.	M. D.	F	24	100	0.18	0.06	1.00	1.30	0.30	0.20	0.20	0.00	+10	Pre-op.
				100	0.16	0.04	0.40	0.80	0.50	0.00	−0.05	−0.05	−32	2 months
39.	R. M.	M	14	95	0.16	0.07	1.60	0.60	0.10	0.30	0.15	−0.10		Pre-op.
				85	0.16	0.08	1.30	0.60	0.00	0.15	0.10	−0.05	−47	1½ months

THE RELATION OF THE VELOCITY OF BLOOD FLOW TO THE BASAL METABOLIC RATE AND TO THE SIZE OF THE HEART

The slowing in velocity of blood flow which generally occurs concomitant with lowering in the basal metabolic rate has been previously described.[6-9] The same relation was evident in patients with angina pectoris and in the subjects without heart disease. (Tables II and III.) In patients with congestive failure in whom the velocity of blood flow before operation was slow, the development of the hypothyroid state was frequently accompanied by a further slowing in the velocity of blood flow. The significance of this, in relation to the clinical improvement shown by these patients, has been discussed in a previous communication.[9]

Of twenty-two patients with congestive failure fifteen showed a correlation between the changes in heart size and the velocity of blood flow. In eight of these fifteen patients the transverse diameter of the heart increased and the velocity of blood flow slowed; in five patients the velocity of blood flow remained slow and the heart size did not change. In two patients the velocity of blood flow increased and the heart became smaller.

BASAL HEART RATE AND BLOOD PRESSURE BEFORE AND AFTER THYROIDECTOMY

Changes in blood pressure and heart rate after total thyroidectomy were variable and striking only in occasional cases.[5, 7] Of thirty-three patients with either congestive failure or angina pectoris eleven showed a decrease, and seven an increase, in heart rate of ten or more beats; fifteen showed changes of less than ten beats per minute (Table VII).

TABLE VII

CHANGES IN BASAL HEART RATE AND BLOOD PRESSURE BEFORE AND AFTER TOTAL THYROIDECTOMY

	HEART RATE	SYSTOLIC B.P.	DIASTOLIC B.P.
Results in 22 patients with congestive failure			
Decreased	6	10	3
No change	11	9	12
Increased	5	1	5
Insufficient data	0	2	2
Results in eleven patients with angina pectoris			
Decreased	5	3	2
No change	4	6	6
Increased	2	0	1
Insufficient data	0	2	2

The above data were analyzed on the basis of changes in heart rate of ten beats or more; changes in systolic blood pressure of 20 mm. or more; and diastolic pressure of 10 mm. or more.

Thirteen patients showed a decrease, and one showed an increase in systolic blood pressure of 20 mm. of mercury or more. Fifteen showed changes of less than 20 mm. of mercury in the systolic pressure. In

four patients data were insufficient. Five patients showed a decrease, and six an increase in diastolic blood pressure of 10 mm. or more of mercury. Eighteen showed changes less than 10 mm. of mercury in the diastolic pressure.

RELATIONSHIP OF CHANGES IN HEART SIZE AND ELECTROCARDIOGRAPH VOLTAGE TO CARDIAC FUNCTION IN PATIENTS WITH ANGINA PECTORIS AND CONGESTIVE FAILURE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

The significance of changes in heart size, basal metabolic rate, electrocardiographic tracings, and velocity of blood flow as expressions of the hypothyroid state has been briefly reviewed. That such changes do not result in impairment in cardiac function has been shown by the striking improvement coincident with the development of the hypothyroid state in patients who, before operation, suffered from chronic heart disease. Objective measurements of the degree of functional improvement in such patients have also been made. A modified Master and Oppenheimer exercise tolerance test[24] was performed by patients with congestive failure before and at varying intervals after thyroidectomy. Patients with angina pectoris undertook similar exercise under the standardized conditions elsewhere described.[32] After the development of the hypothyroid state patients with congestive failure showed a more normal response of blood pressure and heart rate to the same or greater increments of exercise than was evident before operation (Table VIII). Patients who showed marked dyspnea and collapse on exercise before operation experienced little or no distress when the test was repeated after thyroidectomy. Similarly, patients with angina pectoris no longer experienced attacks of chest pain on exercise under conditions which invariably produced anginal attacks before operation, in spite of increases in heart size and diminution in voltage of the electrocardiographic tracings (Table IX). The tests outlined herein are examples of many others to be published in forthcoming publications. The increased capacity for exercise demonstrated by these patients usually paralleled the slowing of the velocity of blood flow as the basal metabolic rate fell.

DISCUSSION

In previous communications the treatment of intractable heart disease by total thyroidectomy was demonstrated as a feasible and effective procedure in patients without clinical or pathological evidence of hyperthyroidism. From previous studies the conclusion had been drawn that by reducing the basal metabolism in patients with heart disease one would lessen the metabolic and circulatory demands of the individual so that the previously reduced circulation would become adequate to the decreased needs of the body.

TABLE VIII

RELATIONSHIP OF CHANGES IN HEART SIZE, ELECTROCARDIOGRAPHIC VOLTAGE, BASAL METABOLIC RATE AND VELOCITY OF BLOOD FLOW TO CARDIAC FUNCTION IN PATIENTS WITH CONGESTIVE FAILURE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE	TIME INTERVAL	TRANSVERSE CARD. DIAM.	HALF CHEST DIAM.	VOLTAGE IN MILLIVOLTS R_2	VOLTAGE IN MILLIVOLTS T_2	B. M. R. PER CENT	VBF IN SEC.	TRIPS	RETURN TO NORMAL IN MINUTES B. P.	RETURN TO NORMAL IN MINUTES PULSE	COMMENT
1.	L. B.	F	44	Pre-op.	13.9	11.0	1.3	0.2	– 9		10	9½	3	Marked dyspnea Finished exercise in 1′ 30″
				6 mo.	15.4	11.1	0.4	0.0	–37		10	2	2	No dyspnea Finished in 1′ 08″
2.	E. W.	M	27	Pre-op.	17.3	15.9	1.0	0.2	+ 5	23	26	8	4½	Collapse, dyspnea 5 min.
											26	7	5	Dyspnea 8 min.
				3 mo.	18.9	16.2	0.8	0.15	–27	52.0	35	5½	3	Slight dyspnea
3.	W. D.	M	22	Pre-op.	17.7	15.0	0.65	0.2	– 8	51	18	–	8	Collapse
											19	–	5	Marked dyspnea, collapse
				3 mo.	17.2	15.1			–27	41	32	2	2	No dyspnea
				5 mo.	18.4	14.8	0.70	0.1	–24	48	24	3	1	No dyspnea

TABLE IX

RELATIONSHIP OF CHANGES IN HEART SIZE, ELECTROCARDIOGRAPHIC VOLTAGE, BASAL METABOLIC RATE AND VELOCITY OF BLOOD FLOW TO CARDIAC FUNCTION IN PATIENTS WITH ANGINA PECTORIS BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE	TIME INTERVAL	TRANSVERSE CARD. DIAM.	HALF CHEST DIAM.	VOLTAGE IN MILLIVOLTS R_2	VOLTAGE IN MILLIVOLTS T_2	B. M. R. PER CENT	VBF IN SEC.	NO. OF TRIPS	RESULT OF EXERCISE
1.	A. B.	M	59	Pre-op.	11.2	14.5	1.2	0.25	− 8	24	58-73	Angina
				6½ mo.	12.9	14.4	0.8	0.0	−31	25	419	No angina
2.	G. O.	M	65	Pre-op.	13.4	15.5	0.2	0.1	−13	15	21-21	Angina
				5½ mo.	14.9	15.0	0.3	0.0	−30	21	50	No angina
3.	R. S.	F	57	Pre-op.	11.3	13.4			+ 3	16	29-30	Angina
				3½ mo.	12.2	13.7			−16	22	60	No angina
4.	M. W.	M	54	Pre-op.	10.4	14.3	0.1	0.5	− 8	19	13-15	Angina
				5½ mo.	11.9	14.7	0.1	0.5	−34	35	75	No angina

The same considerations of supply and demand for blood underlie the rationale for total ablation of the thyroid for relief of angina pectoris. When the work of the heart is augmented, as in exercise, there must be a rise in coronary circulation. If, because of arteriosclerotic narrowing of the coronary vessels or other causes, the coronary circulation cannot increase in accord with the increased needs of the heart, anoxemia develops and angina pectoris ensues.[25] After the development of hypothyroidism following total thyroidectomy, the heart at rest requires less coronary blood flow and can therefore withstand a greater increment of work before reaching the upper limit of circulation set by the relatively fixed coronary vessels.

Since the inception of this work twenty patients with angina pectoris and forty-five patients with various types of congestive failure have undergone operation. With the development of hypothyroidism, most of these patients have shown definite clinical evidence of relief of congestive failure and angina pectoris, notwithstanding changes in heart size and electrocardiographic voltage characteristic of hypothyroidism.

The foregoing observations on artificial myxedema after total thyroidectomy in patients with congestive failure have shown that the changes in heart size are evidently the result of two opposite factors: (1) the effect of the hypothyroid state tending to increase the size of the heart; (2) the restoration of circulatory compensation tending to decrease the size of the heart. The heart size of the individual patients in this group decreased or increased according to which factor predominated. In some patients the two opposing tendencies evidently counterbalanced each other, for the heart size remained unaltered. These variable changes are in contrast to the almost invariable tendency of the heart to increase in size in patients with spontaneous myxedema who had no congestive failure.[21] Similarly electrocardiographic changes typical of myxedema were present in only fourteen of twenty patients with congestive failure.

In patients with angina pectoris in whom the factor of shrinkage of the heart with restoration of circulatory compensation was not operative, and in patients without heart disease in whom artificial myxedema was produced, increased heart size and diminished voltage in electrocardiographic tracings occurred more often. Eight of eleven patients with angina pectoris showed an increase in heart size, and three no change Three of four patients without heart disease showed these changes.

In this study the character, rate, and extent of development of changes in heart size and electrocardiographic voltage coincident with the development of the hypothyroid state could be followed from the time of their first appearance. By means of simultaneous observations of the basal metabolic rate, blood cholesterol, velocity of blood flow, and development of clinical signs and symptoms of myxedema, it was possible

to study accurately the degree of hypothyroidism. It became evident on the basis of these indices that the rate and extent of development of change in heart size and electrocardiographic voltage paralleled the development of the hypothyroid state. These changes were usually not progressive over periods of study as long as three to twelve months if the metabolism was maintained at about minus 30 per cent by the administration of thyroid. Our observations indicate that the increase in heart size and diminution in voltage of the R- and T-waves in the electrocardiogram which occur in myxedema are an accompaniment and an intrinsic characteristic of the hypothyroid state rather than a secondary consequence of myxedema.

These studies also demonstrate clearly that "myxedema heart" in the sense of circulatory failure does not exist as a necessary accompaniment of the hypothyroid state. Most of the subjects of this study had suffered serious cardiovascular disease over an extended period of time and so might have been expected to show more readily any further impairment of cardiac function due to the development of myxedema. In the presence of increased cardiac size and diminished voltage of the electrocardiogram, however, signs and symptoms of congestive failure, rather than becoming more prominent in these patients, disappeared. That the increased cardiac size due to hypothyroidism does not subsequently cause functional impairment is shown by an analysis of the clinical course of patients months after operation. The course of the patients who showed the greatest increase in heart size is of particular interest. Although Patient 1 showed the greatest increase in the transverse cardiac diameter (2.7 cm.), she has experienced striking clinical improvement during the twelve months since total thyroidectomy. Prior to operation she was confined to bed, having had rheumatic heart disease with attacks of congestive failure over a period of twenty-six years. At the time of writing, twelve months after total thyroidectomy, her capacity for work is unmistakably greater than at any time since operation. She is able to perform household duties without dyspnea, is no longer orthopneic, and at no time has evidenced the signs or symptoms of congestive failure. Case 2 was a twenty-seven-year-old man with rheumatic heart disease, hemoptysis for seven years, and attacks of congestive failure for five years. This patient was a cardiac invalid for three years prior to operation. Six months after operation, in spite of an increase in heart size of 2.1 cm., this patient was up and about from eight to ten hours a day without evidence of return of congestive failure. Case 4 was a sixty-six-year-old man with syphilis, arteriosclerotic heart disease, and congestive failure of six years' duration, who had been confined to bed or chair for four years. Eight months after operation, in spite of daily activity, this patient has shown no evidence of congestive failure. This patient showed x-ray and electrocardiographic

changes typical of hypothyroidism. It is apparent that the cardiac enlargement occurring in these patients concomitant with the development of hypothyroidism has not impaired cardiac function.

A similar conclusion may be drawn from a study of the reaction of these patients to exercise. Prior to operation patients with congestive failure performing standard exercise tolerance tests exhibited marked dyspnea, collapse, and an abnormally slow return of blood pressure and pulse to normal after the termination of exercise. After operation, in the face of increased cardiac size and diminution in electrocardiographic voltage, they were able to accomplish even more work with little or no dyspnea and with a more normal physiological response of blood pressure and pulse. Likewise, patients with angina pectoris no longer experienced attacks of pain on exertion in spite of teleroentgenographic and electrocardiographic changes typical of hypothyroidism. One may conclude, therefore, that "myxedema heart" in the sense of a condition aggravating or precipitating attacks of congestive failure or angina pectoris does not exist in patients with induced hypothyroidism in whom the basal metabolic rate is maintained at about minus 30 per cent.

SUMMARY AND CONCLUSIONS

1. Observations are presented concerning the rate and character of changes in heart size in thirty-seven patients, and changes in electrocardiographic voltage in thirty-two patients in whom artificial myxedema was produced by total ablation of the normal thyroid gland. These patients were observed from one and one-half to twelve months after operation.

2. The degree of the hypothyroid state was estimated by measurements of the basal metabolic rate, velocity of blood flow, blood cholesterol, and the signs and symptoms of myxedema. Changes in heart size and electrocardiographic voltage were interpreted on the basis of these indices.

3. After total thyroidectomy, fifteen of twenty-two patients with congestive failure showed an increase of more than 0.5 cm. in the transverse cardiac diameter, three showed no change, and four showed a decrease of more than 0.5 cm. Of eleven patients with angina pectoris eight showed an increase in heart size and three no change; of four patients with no heart disease three showed an increase in heart size and one no change.

4. The variations in changes in heart size in the patients who had congestive failure before operation were the result of two opposing factors: (1) the effect of the hypothyroid state tending to increase heart size; (2) the restoration of circulatory compensation tending to decrease heart size.

5. Observations on the changes in the electrocardiographic voltage

of P- and T-waves in thirty-two patients gave the following results: of twenty patients with congestive failure fourteen showed a decrease, five no change, and one an increase in voltage; of eight patients with angina pectoris five showed a decrease and three no change in voltage; of four patients without heart disease all showed a decrease in voltage.

6. The rate and extent of increase in the heart size and of decrease in electrocardiographic voltage of these patients paralleled the development of the hypothyroid state and were a manifestation rather than a secondary consequence of myxedema. These changes generally showed no progression when the metabolism was fixed at a given decreased level by thyroid medication, and regressed if the metabolism was raised significantly.

7. In spite of these changes in heart size and electrocardiogram, the patients studied showed a disappearance of signs and symptoms of congestive failure or of angina pectoris with persistence of improvement from three to twelve months, and increased capacity for work as measured by standard exercise tolerance tests.

8. "Myxedema heart" in the sense of a condition aggravating or precipitating attacks of congestive failure or angina pectoris does not develop when hypothyroidism is produced by total ablation of the normal thyroid gland in patients whose metabolism is maintained at about minus 30 per cent.

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THE DETERMINATION AND THE SIGNIFICANCE OF THE AREAS OF THE VENTRICULAR DEFLECTIONS OF THE ELECTROCARDIOGRAM*†

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IT IS the purpose of this article to describe a method of analyzing the electrocardiogram which has not been employed hitherto and which yields information not obtainable in other ways. This method is based upon the measurement in suitable units of the areas of the electrocardiographic deflections in the three standard leads. The data so obtained are used to determine the mean electrical axis of the heart during the inscription of the QRS deflections, of the T deflection, and of the ventricular complex as a whole. The mean electrical axis during the inscription of the auricular complex may be determined by the same method.

Methods. We may illustrate this method by applying it to the electrocardiogram reproduced in Fig. 1, which is a characteristic example of the curves seen in bundle-branch block of the common type. In this instance two string galvanometers were employed, and Leads II and III were each recorded simultaneously with Lead I. The original curves, taken on film, were enlarged approximately six diameters by projection. The ventricular complex as it appeared in each lead was then traced (Fig. 2) on thin paper by following the lower margin of the string shadow with a sharp pencil. Due care was taken to place each of the three tracings in its proper relation to the zero level, represented by the horizontal line *HH'*, and to the vertical line *VV'*, which marks the beginning of the QRS interval.

It is desirable that the areas of the electrocardiographic deflections should be expressed in units that do not vary in value with the film speed or with the string sensitivity employed in recording individual curves. The larger rectangles defined by the vertical and horizontal coordinates in Fig. 1 are 5 mm. in height and extend lengthwise over an interval of 0.2 second. Since the introduction of one millivolt into the string circuit produced a deflection of exactly one centimeter, the area of each of these rectangles is equivalent to that of a deflection 100 micro-

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volts in amplitude and one second in duration, or to 100 microvolt-seconds (m.v.s.). The smaller rectangles are each equivalent to four such units of area. After tracing each ventricular complex the corners of the projected image of one of the larger rectangles lying in the same vertical section of the film were marked by small dots, which were subsequently connected by straight lines. Only two such rectangles appear in Fig. 2, because in this instance the even spacing of the time lines made a third unnecessary.

When the tracings were completed, they were mounted on cardboard to prevent creeping of the thin paper, and two vertical lines were drawn, one at the end of the QRS interval and the other at the end of the ventricular complex. The area of QRS and the area of T in each lead were then measured with an accurate planimeter. In measuring the

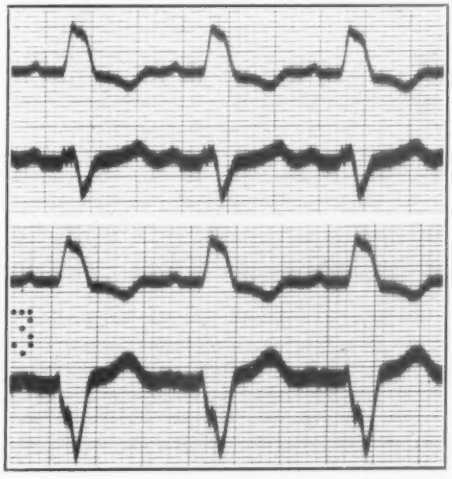

Fig. 1.—Standard electrocardiogram of the type seen in bundle-branch block of the common variety. Upper record: Lead I and Lead II. Lower record: Lead I and Lead III.

former we began at the intersection of the baseline with the line *(VV')* which represents the beginning of the QRS interval, and followed the outline of the curve until the line that marks the end of the QRS interval was reached. This line was then followed to the baseline, and the latter was traced back to the starting point. In measuring the area of T we began at the intersection of the baseline with the line that marks the end of the QRS interval. Passing along this last line to its junction with the outline of the curve, we followed the latter to the end of the ventricular complex and returned along the baseline to the point of beginning. This method of measurement gives the net area; i.e., those portions of the area that lie below the baseline and are considered negative and those that lie above the baseline and are considered positive are added algebraically by the planimeter. The area of QRST, the

ventricular complex as a whole, was obtained by algebraic addition of the area of QRS and the area of T. All areas were then expressed in microvolt-seconds by dividing each of them by one one-hundredth of the area, measured by planimeter in square millimeters, of the large rectangle traced from the corresponding part of the film, and have been arranged in tabular form (Table I).

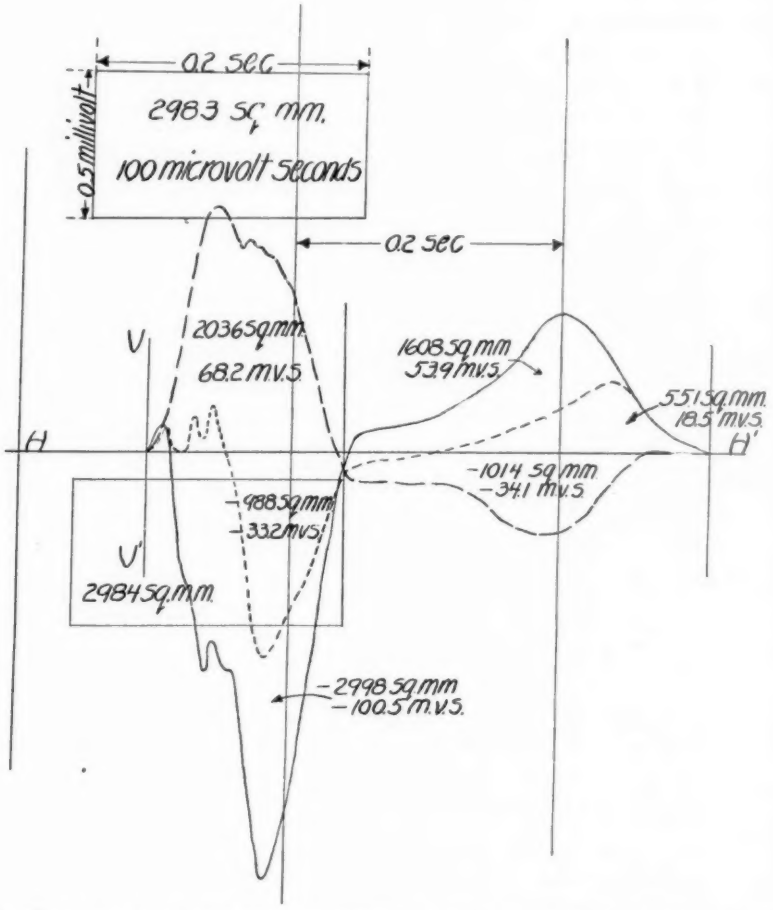

Fig. 2.—Tracings of the ventricular complexes of the curves shown in Fig. 1. The area measurements were made with a planimeter.

TABLE I*

	I	II	III	ANGLE	MANIFEST AREA
QRS	67.3	-33.2	-100.5	-49	102.5
T	-35.7	18.5	54.2	130	55.0
QRST	31.6	-14.7	-46.3	-48	47.2

*Areas in microvolt-seconds of the ventricular deflections of electrocardiogram shown in Fig. 1.

In cases in which the curves have been inaccurately standardized, the appropriate corrections must, of course, be made. It is clear that the area of any deflection or group of deflections in Lead II must equal the sum of the areas of the deflections inscribed in Leads I and III during the same interval. This rule is a necessary consequence of Einthoven's equation, which states that at any instant the deflection in Lead II must equal the sum of the deflections in the other two leads. It is very useful as a check upon the accuracy of the area measurements. It is not essential that two or more leads be taken simultaneously; the method described may be successfully applied when the three leads are taken in rotation in the ordinary way. When this is done, curves which show large respiratory variations in the form of the ventricular complex should be avoided. Otherwise, it may be necessary to measure several complexes in each lead in order to obtain figures in accord with the rule mentioned. In many instances we have made enlarged photographic prints, instead of tracings, of the original curves, and this method is to be preferred as the more accurate. The prints should be mounted to prevent curling. The proper location of the baseline is a matter of the greatest importance. A slight error in placing this line may be responsible for a large error in the measurement of the area of the T-wave which rests upon a broad base. It is therefore best not to attempt to measure curves in which the baseline shifts or in which, for some other reason, its position cannot be exactly determined.

The mean electrical axis and the manifest area. Einthoven and his associates[1] have shown that the resultant electromotive force developed by the heart at any instant may be represented by an electric dipole or doublet located at the center of an equilateral triangle. The right arm, left arm, and left leg are represented by the apices of this triangle, and the three standard electrocardiographic leads by its three sides. The position of the axis of the doublet, which may be referred to as the instantaneous electrical axis of the heart, is defined by the angle α which it makes with the side of the triangle corresponding to Lead I. The potential difference that this doublet would produce in a given lead if its axis were parallel to the corresponding side of the triangle is referred to as E, the manifest potential difference. If a segment of length E is laid off upon the electrical axis, the deflections in the three leads will be given by the projections of this segment upon the three sides of the triangle. When the deflections in any two leads are known, the angle α and the manifest potential difference may be determined by several methods.

If, in like manner, we represent the mean electromotive force developed by the heart during the QRS interval by a doublet at the center of Einthoven's triangle, the axis of this doublet may be referred to as the mean electrical axis of QRS. We may lay off on this axis a seg-

ment *E* equal in magnitude to the manifest area of QRS; i.e., the area of the QRS deflections that would be inscribed in a given lead if the mean electrical axis were parallel to the corresponding side of the triangle. The projections of this segment upon the sides of the triangle will then give the area of QRS in each of the three leads. If the area of QRS is known for any two leads, the inclination of the mean electrical axis of QRS and the manifest area of QRS are easily found. The mean electrical axis of T, the manifest area of T, the mean electrical axis of QRST, and the manifest area of QRST may be defined in the same way and may be found by the same methods. From the center of Einthoven's triangle as origin three vectors, representing QRS, T and QRST, respectively, may then be drawn in such a way that each vector will give the position of the mean electrical axis and the magnitude of the manifest area of the corresponding deflection or group of deflections. The

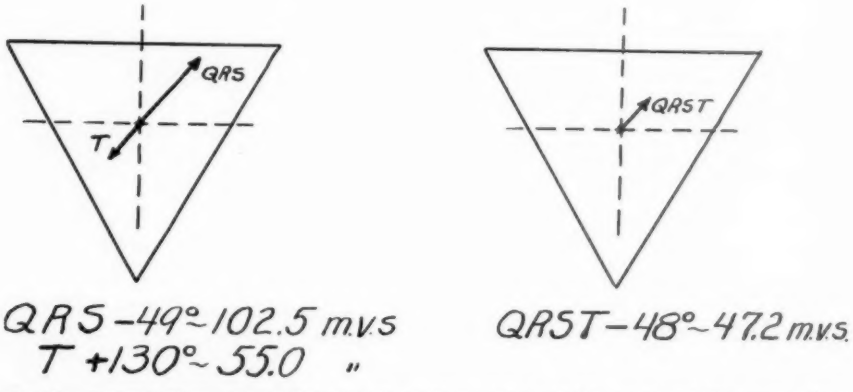

Fig. 3.—The position and relative length of the vectors which represent the mean electrical axis of QRS, of T, and of QRST in Fig. 1.

last of these vectors is the vector sum of the other two. The vectors which represent the QRS, T and QRST deflections of the electrocardiogram reproduced in Fig. 1 are shown graphically in Fig. 3. The angles, which define the directions, and the manifest areas, which give the lengths of these vectors, are set down in Table I in line with the measured areas from which they are derived. It will be noted that although the mean electrical axis of T is separated from that of QRS by an angle of approximately 180 degrees, the manifest area of T is only a little more than half as great as that of QRS. For this reason the mean electrical axis of QRST and the mean electrical axis of QRS have approximately the same direction.

The mean electrical axis and the manifest area of any deflection or group of deflections may be determined with approximately the same accuracy as the electrical axis and manifest potential difference at a given instant. There is no fundamental difference between the method

followed in the determination of the former and that employed in the determination of the latter. Both methods rest upon the same foundations and involve the same assumptions. The mean and the instantaneous electrical axis are both resultants and both involve a process of vectorial summation; the former differs from the latter in that the summation extends over a time interval.

Significance of the mean electrical axis. The significance that is attributed to the mean electrical axis naturally depends upon the interpretation that is placed upon the instantaneous electrical axis. We shall adopt the view, originally advanced by Lewis,[2] that at any instant during the QRS interval the electrical axis points in the direction in which the excitatory process is at that moment spreading along the average ventricular muscle fiber.

This view, which is strongly supported both on the experimental and on the theoretical side[2, 3, 4] advances two distinct and independent postulates. The first of these has to do with the manner in which the electrical forces produced by the various muscle units composing the ventricles are to be summed in order to find their resultant. It is held that so far as the potential differences produced in the three standard leads are concerned, the component electrical forces may each be represented by a vector and may be added vectorially or according to the parallelogram law. The electrical axis of the heart is determined in accordance with this principle, and the assumptions that permit us to add the electrical forces produced in different parts of the heart as if they were vectors are the same as those upon which Einthoven's equilateral triangle is based. In other words, it is assumed that for practical purposes we may consider the apices of the triangle distant and equidistant from all parts of the heart and that we may consider the body a homogeneous conductor.

The second postulate has to do with the relation between the orientation of the electrical forces associated with the wave of excitation and the direction in which this wave is moving. If a constant relation of this kind exists, it must follow that at any instant the effective force produced by a muscle fiber is fully determined within that portion of the fiber which is in the process of passing from the resting to the active state. The extent and position of the remaining portions of the fiber are immaterial. It is implied that if two adjacent elements of a muscle fiber differ in their state of activity, one being nearer to or farther from the resting state than the other, there must be an electromotive force across and normal to the plane that separates them.

Theoretical effects produced by a muscle fiber suspended in air. Bearing these postulates in mind, we may attempt to evaluate the more important factors that determine the areas of the electrocardiographic de-

flections. This purpose will be most easily accomplished by discussing theoretical experiments upon single cardiac muscle fibers. It will be convenient to employ the terminology of the so-called membrane theory, and to assume in accordance with this theory that a resting muscle fiber is surrounded by a polarized* membrane which is partly or completely depolarized when the fiber becomes active, and is repolarized when the fiber returns to the unexcited state.

Let us first consider a curve of the kind obtained by leading directly from muscle strips removed from their natural surroundings and suspended in air. Imagine that it were possible to isolate a single cardiac muscle fiber and place it in contact with two nonpolarizable electrodes

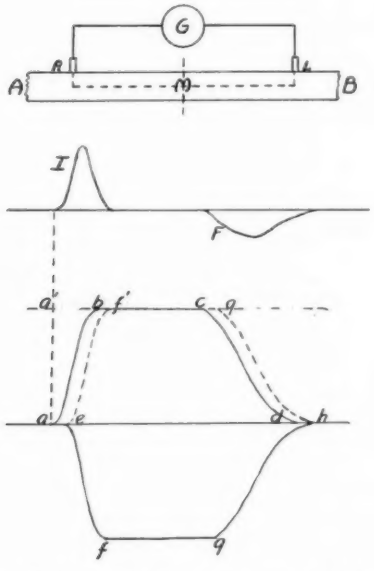

Fig. 4.—Diagram illustrating the electrical effects produced by excitation of a muscle fiber suspended in air.

arranged as in Fig. 4 and connected to the terminals of a sensitive galvanometer or electrometer. For our present purpose we may disregard such complications as arise from the presence of a film of fluid on the outside of the fiber and consider the electromotive force in the galvanometer circuit proportional to the electromotive force in the circuit *GRMLG*, and therefore to the difference between the intensity of

*A membrane or surface may be referred to as polarized when it displays equal and opposite electrical properties on its two sides. A muscle element is polarized when it exhibits equal and opposite properties at its two ends. If a polarized body is placed in an electric field in such a way that the lines of force and the direction in which the body is polarized are perpendicular, the intensity to which a given element of the body is polarized is measured by the moment of the couple acting upon that element divided by the product of its volume and the strength of the field. In the case of a polarized membrane or surface the intensity of polarization may be defined as the electrical moment per unit area per unit strength of field. Across a polarized surface there is an electromotive force proportional to the intensity of polarization[4].

polarization beneath the electrode at *R* and the intensity of polarization beneath the electrode at *L*. If the intensity of polarization is the same at both points, this electromotive force will be zero; if it is less beneath one electrode, that electrode will be relatively negative with respect to the other.

It should be observed that in effect there is an electromotive force across every boundary that defines a difference in the intensity of polarization. If for example, a plane through *M* divides the muscle membrane into two parts, one of which is polarized to an intensity P_1 and the other to an intensity P_2, the electromotive force in all leads from the external surface will be the same as if a surface coinciding with that portion of the specified plane lying inside the fiber were polarized to an intensity P_2–P_1. Where there is a gradient in the intensity of polarization over a given portion of the fiber, the effect is the same as if that portion of the fiber were polarized in a direction parallel to the axis of the fiber.

If the electrodes (Fig. 4) are sufficiently close together, the curve recorded when the muscle is stimulated at *A* will consist of a sharp initial deflection (*I*) corresponding to the QRS deflections of the ventricular complex, and a broader final deflection (*F*) corresponding to the T-wave. This diphasic curve may be considered the algebraic sum of two monophasic curves, one of which (*abcd*) represents the curve that would be obtained if the passage of the excitation wave produced no change in the intensity of polarization beneath the electrode at *L*, and the other (*efgh*) the curve that would be obtained if it produced no change in the intensity of polarization beneath the electrode at *R*. The first of these monophasic curves would actually be recorded if the excitatory process were initiated at *A* and blocked between *R* and *L*. If the excitation wave were blocked between *L* and *B*, the second could be obtained by transferring the electrode at *R* to the latter point. If the electrodes are so close together that depolarization is complete at *L* before repolarization begins at *R*, the initial deflection (*I*) of the diphasic curve may be ascribed to the depolarization, the final deflection (*F*) to the repolarization process.

It is easily shown that if, as a result of the passage of the wave of depolarization or the wave of repolarization along the fiber, the intensity of polarization changes in the same manner and to the same extent beneath both electrodes, the area of the resulting deflection is proportional to the magnitude of the change and to the time required by the process producing it to spread from the first electrode to the second, but does not depend upon the form of the curve that represents the manner in which the change takes place. We may sum the two monophasic curves algebraically by reversing the sign of the second (*efgh*) and subtracting the ordinates of the resulting curve (*ef'g'h*) from those of

the first (*abcd*). The area of the initial deflection (*I*) of the diphasic curve will then be represented by the area *abf'e* and the area of the final deflection (*F*) by the area *cg'hd*. If the curve *ab* and the curve *ef'* are alike in form, the first of these areas is equal to that of a rectangle of which *aa'* is one side and *ae* the other; if the curve *cd* and the curve *g'h* are alike in form, the second area is equal to that of a rectangle of which *aa'* is one side and *dh* the other. It is therefore clear that, provided it does not change from point to point, the form of the curve that represents the manner in which depolarization takes place cannot affect the area of the initial deflection *I*. If the form of the curve that represents repolarization does not vary, it cannot affect the area of the final deflection *F*.

The sum of the areas of the initial and final deflections (*I* and *F*) of the diphasic curve must be equal to the sum of the areas of the two monophasic curves (*abcd* and *efgh*). If the areas of the latter are alike in absolute magnitude, the area of *F* must be equal in magnitude but opposite in sign to the area of *I*, and the sum of these areas must be zero. This sum must always measure the difference in absolute magnitude between the two monophasic curves; if it is not zero, we may conclude that the curve *abcd* and the curve *ef'g'h* differ in form. There is then a difference between the changes in the intensity of polarization produced by the excitation process at *R* and those produced by this process at *L*. Such a difference in the behavior of the muscle beneath the two contacts must depend chiefly, if not entirely, upon factors that do not affect the muscle as a whole but act upon it locally.

Excitation at *R* may differ from excitation at *L* either as regards the magnitude of the change in the intensity of polarization produced, the duration of the excited state, the form of the curve that represents depolarization, or the form of the curve that represents repolarization. A large difference in the magnitude of the change in the intensity of polarization must produce pronounced displacement of that segment of the diphasic curve which is inscribed immediately after the initial deflection (*I*) ends. In our subsequent discussion we shall assume that no such displacement is present and shall speak of the effects produced by local variations in the excitatory process as if they were due solely to a gradient affecting the duration of the excited state; in other words, to a difference between the velocity of the wave of depolarization and the velocity of the wave of repolarization. There is no apparent reason for supposing that the sum of the areas of the two monophasic curves and, therefore, of the initial and final deflections of the diphasic curve is dependent upon the point of stimulation or upon the distance between the electrodes.

Theoretical effects produced by a muscle fiber immersed in a conducting medium. We may think of a muscle fiber as made up of an arbitrary

number of muscle units or elements placed end to end, and of the effects produced by excitation of a muscle fiber as the sum of the effects produced by excitation of the elements of which it is composed. The electromotive force generated by a single element at a given instant is proportional to the difference in the intensity of polarization at its two ends. We may regard the curve *abcd* (Fig. 4) as representing the changes in the intensity of polarization that take place during excitation at one end of the element and the curve *ef'g'h* as representing the changes that occur, after an interval *ae*, at the other end. The electromotive force generated by the element will then be represented by the curve *IF*. The difference in potential between two electrodes in contact with a muscle fiber suspended in air is proportional to the algebraic sum of the electromotive forces generated by all the muscle units lying between the electrodes. Upon this potential difference the electromotive forces generated by the other elements of the fiber have no effect.

If, however, the muscle fiber is immersed in an extensive conducting medium, the situation is entirely different. Every muscle element producing an electromotive force will then contribute in some measure to the potential difference between the electrodes, which may be placed in contact with the fiber or merely in contact with the medium in which it is immersed. The electromotive force produced by a given element may be represented by a dipole or doublet located inside the element and so placed that its axis coincides with that of the muscle fiber. The strength of this doublet must be made proportional to the cross-sectional area of the element, to its length, and to the difference in the intensity of polarization at its two ends. If the medium about the fiber is sufficiently extensive, the effect of the doublet upon the potential of an electrode at any point will vary inversely as the square of the distance from the electrode to the element and directly as the cosine of the angle between the axis of the doublet and the line drawn from the electrode to the center of the element.

Assuming that the relative position of the electrode and the muscle element does not change, the only variable factor among those that determine the effect exerted by the latter upon the potential of the former is the difference in the intensity of polarization at the two ends of the element. Since this varies in accordance with the curve *IF* (Fig. 4), this curve may be regarded as representing the variations in potential of a single electrode, or the variations in the difference in potential between two electrodes, produced by the excitation of a single muscle element. Every curve obtained from a single fiber or from a group of fibers must therefore represent the algebraic sum of a very large number of curves of this type, varying one from another in sign, in amplitude and in phase. We may, therefore, conclude that the sum of the areas of the initial and final deflections of any curve which represents

the excitation of the ventricular muscle is a measure of the effects produced by local variations in the excitatory process, and particularly by local variations in the duration of the excited state.

Effects produced by a muscle fiber located at the center of Einthoven's triangle. Let us suppose that the immersed fiber lies in the wall of the heart, and therefore at the center of Einthoven's triangle. For all practical purposes the electrodes at the apices of this triangle may then be regarded as equidistant from all the fiber elements. We may therefore represent the doublet generated by a given element at a given instant by a vector coinciding in direction with the axis of the doublet and pointing from the negative to the positive pole. The length of this vector must be made proportional to the strength of the doublet at the given instant. The doublet represented by the sum of all the vectors generated by the different elements of the fiber will then represent the electromotive force produced at that moment by the fiber as a whole.

If each elementary vector is given a length proportional to the product of a given interval and the mean electromotive force produced by the corresponding element during that interval, the resultant vector will coincide in direction with the mean electrical axis of the fiber during the given interval and will have a length proportional to the manifest area of the deflections produced by the activities of the whole fiber during that period. If the fiber is of such a length that depolarization of all its elements is complete before repolarization begins at any point, the deflections produced by depolarization and those produced by repolarization will be separable. The areas of the two sets of deflections in the three leads corresponding to the sides of the triangle will then furnish the data necessary for the determination of three vectors representing, respectively, the effects produced by depolarization, the effects produced by repolarization, and the effects produced by local variations in the excitatory process. The last of these vectors will be the sum of the other two.

If the cross-sectional area of the fiber is uniform, the vector which represents the effects produced by depolarization will coincide in direction with, and will have a length proportional to, the sum of the two vectors drawn from the point where the fiber first becomes active, the point of stimulation, to its two ends. This is true whether the fiber is straight or curved. If there are no local variations in the excitatory process, the inverse of this vector will have the same direction and the same relative length as that derived from the areas of the deflections produced by repolarization.

As an example of the effects produced by local variations in the excitatory state, consider those produced by a uniform gradient in the duration of the excited state. The vector which represents the effects produced by this gradient will point from the end of the fiber where

systole is longer toward the end where it is shorter, and will have a length proportional to the difference in the length of systole at the two ends. Neither the direction nor the length of this vector will be affected by the location of the point of stimulation.

An illustration may perhaps contribute to the understanding of the principles involved. Let *AB* (Fig. 5) represent a muscle fiber of uniform cross-sectional area lying in the wall of the heart at the center of Einthoven's triangle. If this fiber is stimulated at *C*, the effects produced by depolarization will be represented by *CD*, which is the sum of the vectors *CA* and *CB;* the projections of *CD* upon the three sides of the triangle will be proportional to the areas of the deflections produced in the three leads by the depolarization process. Suppose that there is a uniform gradient in the duration of the excited state of such kind

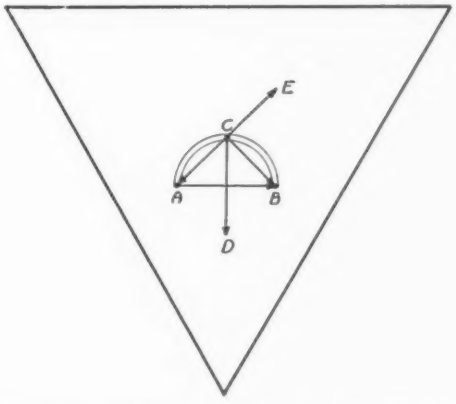

Fig. 5.—Diagram illustrating the electrical effects produced by a muscle fiber lying in the body at the center of Einthoven's triangle (see text).

that systole is longer at *A* than at *B* by an amount equal to the time required by the depolarization process to spread from *A* to *B*. The time required by the repolarization process to spread from *C* to *A* against the gradient (in the direction in which the systole increases in length) will then be double that required by the wave of depolarization, and the effects produced by repolarization of this segment of the fiber will be represented by the vector *AE* which is twice as long as *CA* and opposite in direction. The time required by the repolarization process to spread from *C* to *B* (in the direction in which systole decreases in length) will be zero, for repolarization will begin at *C* and at *B* at the same time. The repolarization of this segment of the fiber will therefore produce no effects whatsoever. The effects produced by the gradient will be represented by *AB*, the vector sum of *AE* and *CD*. The projection of the vector *AB* upon any side of the triangle will be proportional to the sum of the areas of all the deflections produced in the corresponding lead by repolarization and depolarization of the muscle fiber.

It would be possible to extend this discussion to much more complicated cases, but space is not available for that purpose. We have endeavored to make clear the course of reasoning which has led us to the following conclusions: The mean electrical axis of the QRS deflections gives the direction, so far as it can be represented in the plane of Einthoven's triangle in which the depolarization process spreads over the average element of ventricular muscle. The mean electrical axis of T gives the inverse of the direction in which the repolarization process

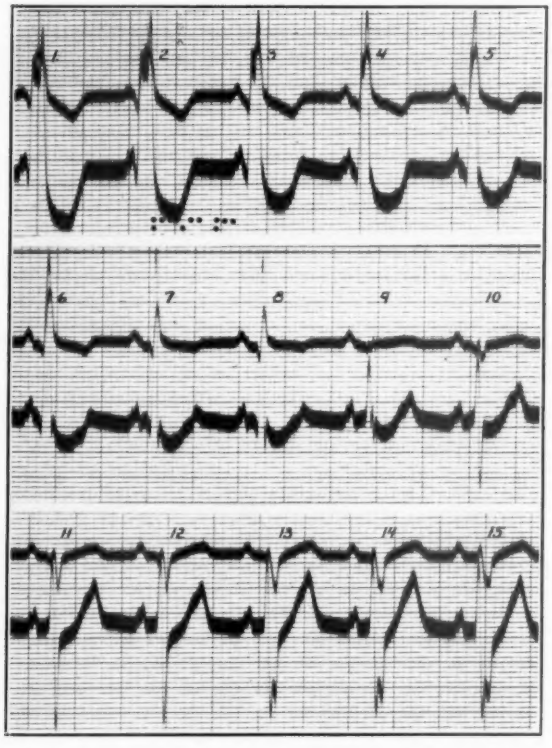

Fig. 6.—A continuous record showing the ventricular complexes referred to in Table II. This series of complexes was obtained by rhythmic stimulation of the central region of the right ventricle after cutting the right branch of the His bundle. Lead I is shown above and Lead III below.

spreads over the average element of ventricular muscle. The manifest area of QRST is a measure of the effects produced by local variations in the excitatory process, and the mean electrical axis of QRST gives the direction of the line along which these variations are greatest. The conclusion that the manifest area and the electrical axis of QRST are determined by local variations in the excitatory process and are not affected by the order in which the various portions of the ventricular muscle pass into the excited state was tested in the following way: A large dog was anesthetized, and the heart was exposed by splitting the

sternum and opening the pericardial sac. The right branch of the His bundle was cut, in the usual way, and the characteristic changes in the form of the ventricular complex were obtained. The central region of the right ventricle was then stimulated rhythmically at a rate only slightly different from the heart rate. In this way a series of ventricular complexes, transitional in form between the complexes of right branch block, and those of the opposite type produced by right ventricular stimulation, were recorded (Fig. 6). Leads I and III were taken simultaneously, and the areas of QRS and T were measured. These areas and the data derived from them are shown in Table II.

It was anticipated that the area of QRST, in both leads, the manifest area of QRST and the mean electrical axis of QRST would remain nearly constant.

The observed variations in these quantities are shown in the table. It will be seen that they are of an irregular kind and show no relation to the form or the area of QRS. They are probably explained by errors in measurement due chiefly to improper placement of the baseline, to the movements of the heart produced by rhythmic inflation of the lungs, and to a lack of uniformity in the movements of the ventricular muscle when contracting. It should also be pointed out that slight variations in the form of the T-wave often occur from beat to beat without obvious cause; these are due, in all probability, to variations in the factors responsible for local peculiarities in the excitatory state.

In judging the significance of the observed variations in the area of QRST, it must be remembered that this area is obtained by the algebraic addition of the area of QRS and the area of T, and is often very small in comparison with the absolute magnitude of the area that must be measured to determine its value. In the case of Complex 2 (Table I) the area of QRST in Lead III was found to be 36.5 m.v.s. The mean value of the area of QRST in this lead was 25.0 m.v.s. The difference between the maximum value (36.5) and the mean value (25.0) is, therefore, approximately 50 per cent of the latter. The former value (36.5) was, however, obtained by measuring the area of QRS, which amounted to 136.0 m.v.s., and the area of T, which amounted to 99.5 m.v.s., a total area of 235.5 m.v.s. An error of 5 per cent in the determination of this total area would therefore account for the maximal variation in the area of QRST above its mean value observed in Lead III. The maximum variation below the mean value (Complex 10) is less easily accounted for. When everything is taken into consideration, however, the data obtained in this experiment will be seen strongly to support the view that the area of QRST is determined by local variations in the excitatory process, and is not dependent upon the area of QRS, which is determined by the order of ventricular excitation.

TABLE II

COMPLEX NO.	LEAD I AREA IN M.V.S.			LEAD III AREA IN M.V.S.			MEAN ELECTRICAL AXIS ANGLE IN DEGREES			MANIFEST AREA IN M.V.S.		
	QRS	T	QRST	QRS	T	QRST	QRS	T	QRST	QRS	T	QRST
1	47.3	−36.0	11.3	132.0	−107.0	25.0	75	−104	72	186.0	149.0	37.0
2	44.7	−35.2	9.5	136.0	−99.5	36.5	76	−105	79	188.0	140.0	48.8
3	40.0	−25.2	14.8	106.0	−82.1	23.9	75	−103	68	152.0	112.0	39.2
4	34.2	−21.9	12.3	98.5	−71.0	27.5	76	−103	72	138.0	97.5	40.7
5	28.4	−19.0	9.4	84.1	−59.7	24.4	77	−104	74	114.0	82.0	34.8
6	25.9	−14.0	11.9	79.2	−53.2	26.0	76	−101	72	109.5	71.2	38.7
7	12.4	−10.9	1.5	50.0	−23.7	26.3	79	−108	87	66.1	35.3	31.2
8	9.9	− 5.3	4.6	40.8	−21.8	19.0	79	−101	79	53.8	28.8	26.1
9	− 2.2	4.9	2.7	13.9	8.7	22.6	98	69	84	15.0	13.7	27.6
10	− 6.6	6.5	−0.1	− 4.4	20.6	16.2	−127	77	90	11.1	28.5	18.7
11	−10.9	11.2	0.3	−17.2	42.7	25.5	−113	79	90	28.4	57.0	29.7
12	−10.3	15.5	5.2	−19.1	38.5	19.4	−110	73	78	30.0	55.6	25.9
13	−16.1	19.1	3.0	−37.2	69.2	32.0	−107	78	86	54.9	92.7	38.8
14	−16.1	18.8	2.7	−40.7	72.5	31.8	−106	79	86	58.5	96.8	38.3
15	−14.1	20.9	6.8	−42.1	60.1	18.0	−104	76	75	58.5	84.2	25.7

SUMMARY

By measuring the areas of the ventricular deflections of the electrocardiogram it is possible to determine the mean electrical axis of QRS, which gives the direction in which the excitatory process spreads over the average element of ventricular muscle, and the mean electrical axis of T, which gives the inverse of the direction in which the recovery process spreads over the average element of ventricular muscle.

If all the ventricular muscle passed through the period of excitation in the same time and in the same way, the area of QRS and the area of T would be equal in absolute magnitude, but opposite in sign, and the area of QRST would be zero. The area of QRST is a measure of the electrical effects produced by local variations in the excitatory process. The mean electrical axis of QRST gives the direction of the line along which these local variations are greatest.

The local variations in the excitatory process which determine the mean electrical axis of QRST are dependent upon factors that act upon different parts of the ventricular muscle with different intensities. They are not materially influenced by the course of the excitatory process over the ventricular muscle.

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STUDIES IN RHEUMATIC HEART DISEASE

An Analysis of 119 Hearts With Special Reference to the Relationship of Auricular Fibrillation to Mitral Valvular Deformity and Certain Rheumatic Tissue Changes*

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THE problem of the causation of auricular fibrillation has been approached by numerous investigators from various points of view. Anatomical studies[1-9] have demonstrated no specific lesion. Experimental and physiological studies[10-15] have developed the idea that auricular fibrillation is essentially a functional disturbance. It is generally conceded, however, that, although it may be a functional disorder, it is found more frequently in hearts that have been structurally altered by disease than in hearts anatomically sound. More recently statistical reports have been made,[16-23] based mainly on clinical studies and with particular emphasis on the varied etiology and prognosis. The general consensus of opinion of these analyses has been that there is apparent no common etiological factor.

In this study the problem has been approached from a different standpoint. By making an essentially structural study of one form of heart disease, namely, rheumatic, an attempt has been made to answer certain questions: 1. What is the relationship of the occurrence of auricular fibrillation to the presence of various grades of mitral stenosis or insufficiency? 2. What relationship has the occurrence of auricular fibrillation to age at death? 3. What relation has the occurrence of auricular fibrillation to the presence and grade of mitral stenosis or insufficiency in the various decades? 4. What relationship has auricular fibrillation to active rheumatic inflammation independent of the grade of valvular deformity? 5. Is there any relationship between the occurrence of auricular fibrillation and the presence of cardiac lesions in addition to mitral valvular deformity? 6. To what extent does auricular thrombosis occur in hearts with auricular fibrillation, and is there a relationship to the degree of stenosis and active inflammation? 7. What is the mode of death of patients with auricular fibrillation, and is there any relationship to the presence of "rheumatic inflammation"?

To lend significance to the answers to these questions, a group of hearts of patients with auricular fibrillation was compared with a larger

*From the Third (N. Y. U.) Division Pathological Service, Department of Pathology, and the Third (N. Y. U.) Medical Division, Bellevue Hospital.

one of hearts of patients dying with sinus rhythm. In this way discernible differences between the two groups may become apparent.

The importance of the problem may be further inferred from the dicta[24, 25] concerning the relative immunity of patients with chronic progressive valvular disease and auricular fibrillation to the development of subacute bacterial endocarditis. A similar immunity has been noted[20, 25, 26, 27] in patients who have *severe* mitral stenosis. Our interest in the problem was stimulated by the study of a recent case[28] which was an exception to the former dictum. At that time we believed that a parallel which is drawn from the infrequency of the association of subacute bacterial endocarditis and advanced mitral stenosis on the one hand, and auricular fibrillation on the other, must take into account the frequency of auricular fibrillation in the various grades of mitral stenosis.

No attempt was made to duplicate the work of others who have studied the neuromuscular tissue, particularly of the sinus node, or its blood supply, or the nature of auricular lesions in various types of heart disease.

MATERIAL AND METHODS OF STUDY

One hundred and nineteen rheumatic hearts obtained at necropsy during the past thirteen years from the Third (New York University) Medical Division, Bellevue Hospital, were examined. Under this term are included those specimens exhibiting evidences of varying degrees of valvulitis in association with interstitial, vascular, or serosal inflammatory changes or their end-results, in which *no* evidence was found of any *demonstrable or specific bacterial inflammatory change or purely degenerative alterations.*

While the sample is small for purposes of accurate statistical analysis, it is large, nevertheless, when considered from the standpoint of cases coming to necropsy from one medical service.* We are using the data for the trends that analysis may reveal.

All the specimens exhibited some degree of involvement of the mitral valve. Not all were from individuals who were known to have suffered from heart disease in life. The majority (75 per cent) died of congestive heart failure; the rest of a variety of diseases. All cases of bacterial endocarditis were omitted, however, regardless of antecedent changes. Specimens of so-called pure aortic valve involvement were rejected because the etiology could not be determined. Forty-two hearts were from cases of established auricular fibrillation (not paroxysmal); of these, 36 were verified by electrocardiograms. In 27, fibrillation was present for more than one month prior to death, in some instances for several years, and in the majority for more than six months. Of the other 9 cases which had been electrocardiographed, auricular fibrillation

*With an average bed capacity of 150; material has also been drawn from the pediatrics service (average bed capacity of 140) in the past two years since its affiliation with New York University.

was observed in 7 for from one to three weeks before death; the remaining 2 patients died shortly after admission (two to six days) without a reliable history as to the approximate onset of fibrillation. For purposes of this report, 2 cases of established auricular flutter are included, one of three months' the other of one year's duration.

Sex Incidence.—Of the 42 patients with auricular fibrillation, 21 were males and 21 females. Among the 77 cases of sinus rhythm, 51 were males and 26 females. The sex incidence, therefore, is similar to that in recent clinical studies.[21, 23, 29]

Age.—The average age at death of the 42 patients with auricular fibrillation was forty-three years; the youngest was ten, the oldest seventy years of age. The average of those with sinus rhythm was thirty-five years; the extremes were seven and eighty years. Because of limited pediatric necropsy material, the number of hearts from children was small. (Table II shows the distribution of cases according to decades.)

Incidence of Auricular Fibrillation in Mitral Stenosis.—Ninety-six of the 119 specimens exhibited some degree of mitral stenosis. In 39 (40 per cent) auricular fibrillation was present. In the clinical study of DeGraff and Lingg,[23] 50.5 per cent of their 402 rheumatic cardiac patients with mitral stenosis developed auricular fibrillation. Of 100 cases of mitral stenosis reported by Stone and Feil[29] auricular fibrillation occurred in 53 per cent. Weiss and Davis[30] in their report,* including paroxysmal auricular fibrillation or flutter, found an incidence of 57 per cent in 164 necropsied cases of "the most advanced type of rheumatic cardiac change."

Criteria for Pathological Diagnosis.—The grade of stenosis was estimated as severe, and slight to moderate. This was an arbitrary grouping, depending upon the diminution in size of the auriculoventricular orifice. We have found no single criterion or measurement satisfactory for estimating the degree of stenosis. Anyone who has attempted to establish the degree of stenosis by measurement is aware of the difficulties encountered. For example, one sees stenotic orifices which are caused by fusion of only slightly thickened cusps, the ring of the valve remaining within normal limits (Fig. 1). Conversely, one encounters

*The report by these authors deals with material which is considerably different from that presented here. Their finding of "only 66 cases of mitral stenosis of the total 164 cases of marked rheumatic heart disease" is at such variance with our data that strict comparisons may not be made. As already stated, of 119 consecutive hearts of the rheumatic type examined by at least one, and in 90 per cent by all of us, mitral stenosis was encountered in 96 cases, mitral insufficiency 7 times, and in 16 cases inflammatory disease of the mitral valve, although present, was not associated with stenosis or insufficiency of the AV orifice.

To indicate that the discrepancy is not confined to material described here, reference may be made to the anatomical studies of valvular disease of Clawson, Bell and Hartzell[31]. In a group of 166 hearts which may be termed of the rheumatic type, 18 were cases of acute rheumatic endocarditis without valvular defects; 18 were identified as recurrent rheumatic, and 130 were classified under the term old valvular defects. If 32 cases of isolated aortic valve disease and three of isolated pulmonary valve involvement are omitted on the grounds of indeterminate etiology, a group of 131 hearts is set up which may be considered examples of severe rheumatic heart disease. Of these 88 had mitral stenosis, 201 mitral insufficiency, 1 aortic insufficiency, and in the others disease produced no stenosis or insufficiency.

long, narrow, slitlike orifices in which the circumference, as a result of cicatricial shortening of the cusps, approaches that of the ring (Fig. 2). Although both measurements may be practically normal, the degree of stenosis may be severe due to scarring and fixation in position of the cusps. The final decision was based, therefore, upon all the factors contributing to anatomical diminution of the auriculoventricular orifices, such as the size of the valve opening compared to the size of the ring, the degree of approximation of the valve cusps to each other, the degree of fusion of the commissural junctions, fixation in position, and the presence or absence of free motion of the valve. (See Figs. 3 to 6.)

Fig. 1. Fig. 2.

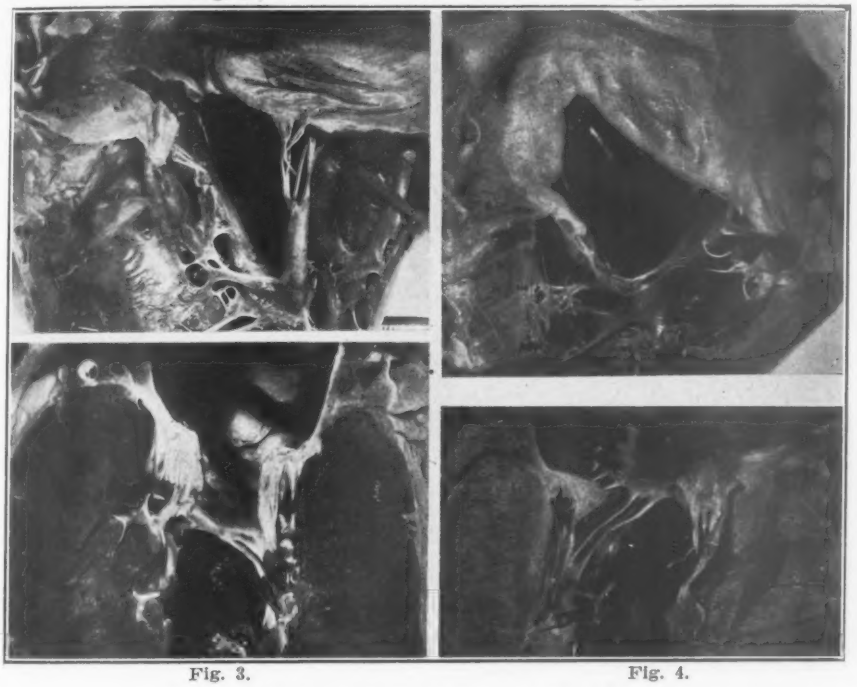

Fig. 3. Fig. 4.

Figs. 1-4.—Severe atrioventricular valvular stenosis.

Fig. 1.—(Necropsy No. 16,573) Female, thirty-eight years. Severe "button-hole" type of stenosis of the tricuspid valve due to obliteration of the commissures by fusion of the cusps. The leaflets are only slightly thickened; the chordae tendineae are somewhat thickened but not shortened. The circumference of the valve orifice is much smaller than that of the ring.

Fig. 2.—(Necropsy No. 12,251) Female, thirty-seven years. Severe "fish-mouth" type of tricuspid stenosis due to fusion at the commissures and marked rigidity of the valve as a result of fibrosis. Because of the retraction of the leaflets with shortening, the circumference of the slitlike orifice approaches that of the ring. The chordae tendineae, most of which are not visible in the photograph, are only slightly thickened and of normal length.

Fig. 3.—(Necropsy No. 19,889) Male, fifty-three years. "Funnel" type of severe mitral stenosis with cicatricial contraction of both leaflets as well as their chordae tendineae. Although there is some retraction of the cusps, the orifice is markedly diminished because of the complete fusion at the commissures and fixation of the leaflets. In this instance the valve ring is of normal circumference, but the valve margins are approximated to produce the diminution of the orifice.

Fig. 4.—(Necropsy No. 17,384) Male, fifty-one years. An example of severe stenosis of the mitral valve with the same relationship of orifice to ring as in Fig. 2 but with more marked scarring and rigidity of the cusps. Here, too, the chordae tendineae, although slightly thickened, are not appreciably shortened.

In addition to the 96 specimens with some degree of stenosis, there were 16 specimens showing mitral valvulitis without stenosis (Fig. 7). There was a third group of 7 specimens in which the mitral valve was considered to be anatomically insufficient. In them there was fusion of the commissures with marked retraction of the leaflets and shortening of the chordae tendineae. In some instances adhesion of the posterior

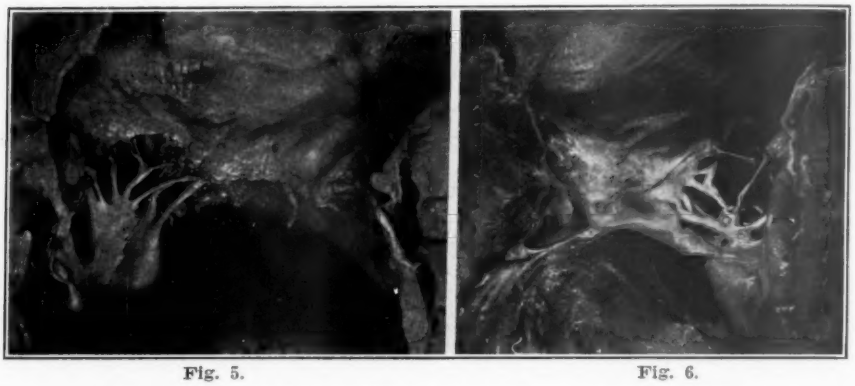

Fig. 5. Fig. 6.

Figs. 5 and 6.—Mild to moderate atrioventricular valvular stenosis.

Fig. 5.—(Necropsy No. 15,687) Male, seventeen years. This photograph illustrates mild stenosis of the mitral valve due to thickening of the leaflets with partial fusion at the commissures but with definite retraction of the cusps so that the circumference of the margin approximates that of the ring. Several chordae tendineae are fused and shortened, and practically all are thickened.

Fig. 6.—(Necropsy No. 17,445) Male, seventy-three years. An example of moderate stenosis of the mitral valve due to cicatricial shortening with fusion of the chordae tendineae. The cusps are only slightly fused at the commissures and only moderately sclerotic.

Fig. 7.—Valvulitis without deformity. (Necropsy No. 10,302) Female, fourteen years, who died during first attack of rheumatic fever. The photograph presents verrucous endocarditis of the leaflets of the mitral valve without deformity. Although the valve is somewhat edematous, there is no encroachment on the lumen. Most of the chordae tendineae are normal in length and thickness.

cusp to the adjacent wall was found (Fig. 8). These changes made valvular closure and stenosis impossible. The finding of various grades of auricular dilatation and the presence of endocardial pockets in the wall of the left auricle with apertures facing the valve orifice were accepted as further anatomical evidence of regurgitation.

Ninety-two hearts were available for complete histological study. (Blocks were taken after the standardized procedure of Gross, Antopol and Sacks[32] consisting of 10-12, and in most instances 15-18, which included the following sites in the heart: all valves and valve rings, pericardium of the left and right ventricles, left and right auricles, myocardium of the left and right ventricles, the interventricular septum, papillary muscles, base of the aorta and pulmonary artery, the neuromuscular bundle, and the coronary sinus.)

The diagnosis of active rheumatic inflammation[33-39] was based on the finding of Aschoff bodies with collagenous necrosis or active valvulitis (nonbacterial), either superficial (verrucous), deep, or both, with or without active pericarditis. Various types of diffuse, nonbacterial valvulitis when associated with varying degrees of myocardial interstitial cellular deposits, especially those adjacent to blood vessels, varying from the Aschoff body to collections of lymphocytes, plasma cells, eosinophiles, polymorphonuclear leucocytes, basophilic mononuclear leucocytes and histiocytes, were also considered positive evidence of active rheumatic inflammation. Recent vascular lesions,[35, 40-43] particularly in the aorta, pulmonary artery and smaller vessels of other organs, when associated with carditis, were considered evidence of active inflammation. Cases were regarded as inactive (healed) when we found

a. *b.*

Fig. 8.—Mitral insufficiency. (Necropsy No. 17,539) Female, twenty-four years. An example of anatomical mitral insufficiency in which there is definite thickening of the valve leaflets with retraction and adhesion of the posterior leaflet to the underlying mural endocardium. The chordae tendineae are only mildly thickened and practically normal in length. The circumference of the valve margin almost equals that of the ring (10 to 10.5 cm.).

(*a*) A view of the intact mitral orifice as seen from above. The auricle was also markedly dilated.

(*b*) This view presents the valve after section through the midportion of the posterior leaflet to show the retraction of this cusp in particular and its fusion to the underlying ventricular wall. The arrow points to a pocketlike structure in the endocardium of the left auricle.

perivascular and intrafascicular scarring of the myocardium, scarring and deformity of the valves with vascularization, without microscopic evidence of active inflammation as described, healed pericarditis, healed aortitis, the latter two findings with characteristic lesions elsewhere.

Several of the specimens which appeared to be inactive grossly presented definite evidence histologically of active inflammation, which reemphasizes[36-38] the need for careful and complete histological studies in deciding on the presence of active rheumatic inflammation. Conversely, what appeared to be verrucae grossly, on histological study proved occasionally to be healed lesions. For this reason the data are analyzed from the standpoint of rheumatic inflammation only in the 92 hearts which were available for histological study.

ANALYSIS OF MATERIAL

First, *what is the relationship of the occurrence of auricular fibrillation to the presence of various grades of mitral stenosis or insufficiency?* About half of each rhythmic group was associated with severe stenosis, and about one-third to one-fourth with mild to moderate stenosis, suggesting that the *rhythm bore no relationship to the grade of stenosis.* It appears that mitral stenosis or organic insufficiency is necessary, however, for the development of *persistent* auricular fibrillation in *rheumatic* heart disease, since there were no cases without significant mitral valvular deformity (Table I).

TABLE I

RHEUMATIC HEARTS. DISTRIBUTION OF CASES ACCORDING TO RHYTHM AND GRADE OF MITRAL VALVE DEFORMITY

MITRAL VALVE DEFORMITY	AURICULAR FIBRILLATION		SINUS RHYTHM		TOTALS	
Severe Stenosis	24	(57%)	38	(49%)	96	(81%)
Mild—Moderate Stenosis	15	(36%)	19	(25%)		
Insufficiency (organic)	3	(7%)	4	(5%)	7	(6%)
None			16	(21%)	16	(13%)
Total	42		77		119	

Second, *what relationship has the occurrence of auricular fibrillation to age at death?* Of 42 hearts from cases of auricular fibrillation, two-thirds were from patients over forty years of age; whereas, of the 77 specimens from cases of sinus rhythm, about one-third was from individuals over forty years of age (Table II). The average age at death, as already stated, was forty-three years in the former. Auricular fibrillation was encountered, therefore, in patients dying with rheumatic heart disease with greater frequency after than under the age of forty. These figures differ somewhat from those given in the clinical studies of Stroud, Laplace and Reisinger[21] and DeGraff and Lingg.[23] In the former, 35.2 years was the average age at death in rheumatic heart disease with auricular fibrillation; in the latter it was 40 years.

This material differs sharply, however, from that employed clinically. One reason for the difference may be that a rheumatic etiology was not known or even suspected in many cases during life. The clinical studies may be deficient in the number of older individuals, since auricular fibrillation, as is well known, makes the precise diagnosis of mitral stenosis difficult. This series includes patients, furthermore, of all age groups whose death was not caused directly by heart disease.* The clinical studies were limited in all probability to patients treated because they were suffering from heart disease and did not include ambulatory

*Several of the patients died of lobar pneumonia, some of cerebral hemorrhage, others of acute appendicitis, carcinoma of the stomach, carcinoma of the breast, acute and chronic diffuse glomerular nephritis, Henoch's purpura, Graves' disease, sepsis, and fractured skull.

patients unaware of its presence. Cases of bacterial endocarditis were also, as already stated, omitted from this series. In a recent report of Stone and Feil[29] of 100 autopsied cases of severe mitral stenosis, the average age was 40.6 years.

Third, *what relation has the occurrence of auricular fibrillation to the presence and grades of mitral stenosis and insufficiency in the various decades?* When the grades of stenosis in the specimens from the auricular fibrillation group were compared as to frequency under and over

TABLE II

MITRAL VALVE DEFORMITY. CASES ARRANGED ACCORDING TO DEGREE OF DEFORMITY AND AGE IN DECADES

MITRAL VALVE DEFORMITY	CASES OF AURICULAR FIBRILLATION						CASES OF SINUS RHYTHM							
	DECADES						DECADES							
	II	III	IV	V	VI	VII	I	II	III	IV	V	VI	VII	VIII IX
Severe Stenosis	1	4	5	5	6	3		6	7	14	6	3	1	1
Mild—Moderate Stenosis	1	2	1	6	2	3		4	1	2	3	4	4	1
Insufficiency	1	1			1		1	2	1					
Total	3	7	6	11	9	6	1	12	9	16	9	7	5	2
	16			26			38				23			
None	0	0	0	0	0	0	0	5	2	4	2	2	0	1

	Under 40	Over 40	Under 40	Over 40
Severe	10	14	27	11
Mild—Moderate	4	11	7	12
Insufficiency	2	1	4	0
No stenosis	0	0	11	5

forty years, stenosis in the younger group was more often severe than mild (10 of 14 specimens, ratio of 2.5:1), while over forty years the incidence approached equality (14 to 11 hearts). In the sinus rhythm group, however, severe stenosis was encountered even more frequently under the age of forty (27 to 7, ratio 4:1), over forty years it was like the fibrillating group (11 to 12, ratio 1:1) (Table II). There is, in short, no relation between the existence of auricular fibrillation and the grade of stenosis in various decades. Most cases of severe stenosis under forty years fall, moreover, in the sinus rhythm group (27 to 10).

Fourth, *what relationship has auricular fibrillation to active rheumatic inflammation independent of the grade of valvular deformity?* Of those cases of auricular fibrillation which were studied microscopically, 17, about half, exhibited some grade of valvular deformity and showed

active inflammation; whereas, of 48 cases of sinus rhythm with some grade of valvular deformity, 30, or three-fifths, presented evidence of active inflammation (Table III).

Evidence of rheumatic inflammation in cases of auricular fibrillation was present in all 12 specimens under the age of forty years, and in 5 of 19, or one-fourth, over the age of forty years. This group is necessarily small, because only those cases were admitted in which a histological study was made. In cases of normal rhythm, evidence of inflammation (activity) was seen in 34 of 41 hearts under forty years and in 8 of the 20 specimens from patients over forty years. It is interesting that of the 12 cases of auricular fibrillation under forty years which were studied histologically, 9 showed active myocarditis, and of these 7 had Aschoff bodies; whereas of the 19 cases over the age of forty years studied histologically only 4 had active myocarditis and of these 2 had the submiliary myocardial nodules. In the sinus rhythm group of 41 cases under forty years, 25 showed active myocarditis and in 21 of these Aschoff bodies were found; while of those over forty years, 5 exhibited active myocarditis and in one there were nodules. These findings suggest that in older subjects active rheumatic inflammation is not a determining factor in the development of auricular fibrillation.

When the grade of severe stenosis in relationship to activity is studied, active inflammation was found in a ratio of 1.4:1 (10 to 7) in the fibrillation group, and in cases of sinus rhythm, in a ratio of 2:1 (20 to 12). In moderate stenosis, activity was found in 5 of 11 specimens from cases of fibrillation and in 6 of 12 of sinus rhythm. Of 53 cases under forty years there were no inactive cases among the fibrillators, whereas in the sinus rhythm group there were 7. Past the age of forty years in both rhythmic groups there were 39 cases, and of these 26 were inactive by the criteria used. This may be interpreted as showing that *under forty years auricular fibrillation may be a manifestation of rheumatic activity in the presence of rheumatic structural* cardiac changes in individuals dying in congestive heart failure.

No special histological features were found differentiating the hearts of the fibrillating from those of the sinus rhythm group. A strict histological comparative examination of the auricles has not been made, however, in this study.

Fifth, *is there any relationship between the occurrence of auricular fibrillation and the presence of cardiac lesions* in addition to mitral valvular deformity?* For the answer to this question the gross material of 119 specimens has been analyzed again (Table IV). In the auricular fibrillation group 57 per cent and in the sinus rhythm group 51 per cent showed significant associated cardiac lesions. Aortic valve deformity occurred more frequently in the sinus rhythm group (30 times against

*The other cardiac lesions, both valvular and pericardial, were examined and classified using the same criteria employed in the study of the mitral valve.

TABLE III

RHEUMATIC ACTIVITY. RELATION TO RHYTHM AND DEGREE OF MITRAL VALVE DEFORMITY ACCORDING TO AGE
(BASED ON HISTOLOGICAL STUDY)

Degree of stenosis	DECADE	AURICULAR FIBRILLATION II	III	IV	V	VI	VII	SINUS RHYTHM I	II	III	IV	V	VI	VII	VIII IX	ACTIVITY IN BOTH GROUPS COMBINED
Severe	active	1	4	4	1				6	4	8	2				30
	inactive				1	4	2			1	4	3	2	1	1	19
Mild—Moderate	active	1			4				2			1	1	2		11
	inactive				1	2	3				2	1	1	1	1	12
Mitral insuff.	active	1	1					1	2	1						6
	inactive					1										1
No valve deformity	active								4	2	4		1		1	12
	inactive												1			1
	Total	3	5	4	7	7	5	1	14	8	18	7	6	4	3	92
			12			19			41				20			

31 cases all with defects of mitral valve studied microscopically.
17 active 14 inactive

48 cases *with* mitral valve defect studied microscopically.
30 active 18 inactive
13 cases *without* mitral valve defect studied microscopically.
12 active

17). It is interesting to note that the *relative* incidence in *each rhythmic* group for aortic valve involvement is about the same (40 per cent). The same is true of combined aortic and mitral valve disease. Adherent pericardium occurred more frequently in the sinus rhythm group (14 times against 7).

TABLE IV

DISTRIBUTION OF CASES OF MITRAL VALVE DEFORMITY WITH AND WITHOUT ASSOCIATED CARDIAC LESIONS ACCORDING TO LESION, RHYTHM AND THE PRESENCE OF RHEUMATIC ACTIVITY

CARDIAC LESIONS	AURICULAR FIBRILLATION			REGULAR SINUS RHYTHM		
	ACTIVE*	INACTIVE*	TOTAL†	ACTIVE*	INACTIVE*	TOTAL†
Mitral and aortic stenosis	4	5	10	13	2	18
Mitral stenosis; aortic insufficiency	1		1	1	1	2
Mitral and tricuspid stenosis	1		2			1
Mitral and tricuspid insufficiency	1		1			
Mitral, aortic, and tricuspid stenosis	1		3	1	1	2
Mitral stenosis; adherent pericardium			3		1	2
Mitral insufficiency; adherent pericardium				3		3
Mitral and aortic stenosis; adherent pericardium	1	1	2	3	2	5
Mitral and tricuspid stenosis; adherent pericardium	1		1			
Mitral, aortic, and tricuspid insufficiency; adherent pericardium				1		1
Mitral, aortic, and tricuspid stenosis; adherent pericardium	1		1			
No mitral valve deformity; adherent pericardium				1	1	3
No mitral valve deformity; aortic insufficiency				2		2
Mitral stenosis	5	7	16	8	11	27
Mitral insufficiency	1	1	2			
Mitral valvulitis with no deformity				9		11
Totals	17	14	42	42	19	77

* = Studied histologically.
† = Includes cases studied macroscopically only.

Cases showing organic disease of tricuspid valve (stenosis, insufficiency, or both) were encountered more often in the relatively small auricular fibrillation group than in the much larger sinus rhythm group (8 times against 4).

In the sinus rhythm group the majority of hearts (26 of 39) with multiple lesions appeared below the age of forty years. (Table V.) In the auricular fibrillation group they were, however, evenly divided above and below forty years. Cases were found in both groups late in life. (Table VI.) More active cases with multiple cardiac lesions were found in the sinus rhythm group than among the fibrillators, under the age of forty years. (Table V.) The relative incidence, however, of active cases in each rhythmic group was the same. There was only one case with multiple lesions under forty years which was inactive, and it fell in the sinus rhythm group. In contrast there were 7 inactive among 12 uncom-

plicated cases of mitral stenosis in the sinus rhythm group under the age of forty years. As already stated, *all* the cases under forty years among the fibrillating group were active.

TABLE V

MITRAL VILVE DEFORMITY. COMPARISON OF CASES WITH AND WITHOUT ASSOCIATED CARDIAC LESIONS ACCORDING TO PRESENCE OF RHEUMATIC ACTIVITY, RHYTHM, UNDER AND AFTER AGE 40

		AURICULAR FIBRILLATION		SINUS RHYTHM	
		UNDER 40	AFTER 40	UNDER 40	AFTER 40
Hearts with multiple lesions	Gross cases	12	12	26	13
	*Active	9	2	21	4
	*Inactive	0	6	1	7
Hearts with mitral valve deformity alone	Gross cases	4	14	15	12
	*Active	3	3	5	3
	*Inactive	0	6	7	4

*Includes only cases studied histologically.

TABLE VI

MITRAL VALVE DEFORMITY. DISTRIBUTION IN DECADES OF CASES WITH AND WITHOUT ASSOCIATED CARDIAC LESIONS

AURICULAR FIBRILLATION			SINUS RHYTHM	
MITRAL VALVE ALONE	MITRAL VALVE AND ASSOCIATED LESIONS	DECADES	MITRAL VALVE ALONE	MITRAL VALVE AND ASSOCIATED LESIONS
		1-10		1
	3	10-19	3	11
4	3	20-29	4	5
	6	30-39	8	9
6	5	40-49	4	5
5	4	50-59	3	6
3	3	60-69	4	1
	0	70-80	1	1

Sixth, *to what extent does auricular thrombosis occur in hearts with auricular fibrillation, and is there a relationship to the degree of stenosis and active inflammation?* Thrombi were observed in one or both auricles, or in their appendages in 12 per cent (15 of 119) of all the cases; 10, or 24 per cent, in the auricular fibrillation group, 9 exhibiting signs of active rheumatic inflammation, and 5 in the sinus rhythm group, 3 being active. Combining both groups, 14 of the 15 specimens presented some degree of mitral valvular deformity. Nine showed severe, 5 mild to moderate stenosis, and 1 showed anatomical mitral insufficiency. In the auricular fibrillation group, 6 of the 10 hearts exhibited severe stenosis; in the sinus rhythm group, 3 of the 5 specimens. (Table VII.)

The average age in the auricular fibrillation group with auricular thrombosis was 39.7 years, the extremes being 18 and 52 years; that in the sinus rhythm group was 41.8 years, the extremes 17 and 63. Three-fourths of all the cases occurred in individuals past forty years of age.

Seventh, *what is the mode of death of patients with auricular fibrilla-*

tion, and is there any relationship to the presence of "rheumatic inflammation"? In fibrillation, congestive heart failure was the mode of death in 88 per cent, whereas in sinus rhythm, it was 68 per cent. Approximately half of each group presented histological signs of active rheumatic inflammation. It is of special interest that in the group with auricular fibrillation under the age of forty years all died in congestive heart failure and showed evidence of active rheumatic inflammation.

TABLE VII

AURICULAR THROMBOSIS IN BOTH RHYTHMIC GROUPS

RHYTHM	NO. OF CASES	VALVE DEFORMITY			RHEUMATIC INFLAMMATION	
		SEVERE STENOSIS	MODERATE STENOSIS	INSUFFICIENCY	ACTIVE	INACTIVE
Auricular fibrillation	10	6	3	1	9	1
Regular sinus rhythm	5	3	2	0	3	2

Evidence of active inflammation was found also in all the sinus rhythm cases, with one exception, under forty years dying in congestive failure. The exception was an inactive case with acute heart failure occurring during labor and associated with paroxysmal tachycardia.

The mode of death in the younger patients is undoubtedly referable to the more diffuse involvement of the myocardium by the inflammatory process. As stated in the answer to question 4, active myocarditis and Aschoff bodies are rare findings in the individual past forty years and are all too common in those under this age. The older individuals must, therefore, be suffering from the effects of disease states superimposed on the old rheumatic tissue changes, degenerative changes, or the wearing out effects of long-standing organic defects of the heart, as well as disorders of rhythm.

COMMENT

It becomes apparent from the data presented that a number of factors play a rôle in the development of *persistent* auricular fibrillation in rheumatic heart disease. While the grade of stenosis of the mitral valve orifice was not found to be related to the presence of *established* auricular fibrillation, some degree of valvular deformity appears to be requisite for its appearance (Table I). To reiterate, cases of paroxysmal auricular fibrillation were not included.

In the material studied, patients over 40 years with auricular fibrillation were encountered more frequently (26 against 16) than were those under this age, and more frequently (62 per cent against 36 per cent) than cases of sinus rhythm (Table II). Further, cases with mitral valvular deformity over the age of forty years occurred more frequently in the auricular fibrillation group (26 against 23). These deductions tend to show that age (including the duration of the disease) may play a determining rôle in the development of the abnormal rhythm.

Of particular interest, though the cases are few, is the analysis of the distribution of active cases. All the patients under the age of forty years with auricular fibrillation showed active rheumatic carditis; in contrast, 17 per cent were inactive in the sinus rhythm group. Since all of the active cases in the auricular fibrillation group died with some degree of congestive failure and showed widespread carditis, it may be reaffirmed that active rheumatic inflammation either precipitates congestive failure or by progressive myocardial impairment leads to its development. This is of importance in a consideration of prognosis and the treatment of young patients.

The presence of active rheumatic inflammation in the younger patients with auricular fibrillation may shed some light on the immune processes and the development of subacute bacterial endocarditis. This immunity is apparent and may be due merely to the fact that they are suffering from an antagonistic state, namely, active rheumatic carditis. This explanation does not apply to cases over forty years, since fewer active cases were found past middle life. However, the recent evidence of Saphir and Wile,[45] a report of cases of subacute *bacterial* endocarditis in children and young adolescents showing coexisting rheumatic tissue changes, indicates need for caution in using anatomical evidence to test an immunological hypothesis.

Directly related to this question is the apparent immunity to bacterial endocarditis of patients with high-grade mitral stenosis. Fulton and Levine[27] have already expressed the opinion, similar to that in the preceding paragraph, that this immunity is based on the persistence of a local rheumatic process in the mitral valve which might be antagonistic to the development of bacterial endocarditis. A study of 49 cases of severe mitral stenosis lends support to this view (Table III). The active were to the inactive as 30 is to 19, a ratio of 1.5:1.

No relationship has been found between the two types of relatively immune hearts; that is, those with auricular fibrillation and those with severe mitral stenosis. This point is to be emphasized in view of the opinion expressed by Stone and Feil[29] that the rarity of auricular fibrillation in subacute bacterial endocarditis may be explained in part by the rarity of subacute bacterial endocarditis in advanced mitral stenosis, arguing that auricular fibrillation is definitely more common in mitral stenosis, especially in advanced cases. It is to be seen, however, that the incidence of auricular fibrillation in their own selected group of 100 cases of severe mitral stenosis was 53 per cent, and no mention is made concerning the duration of the abnormal rhythm. Further, no distinction is made between the occurrence of auricular fibrillation as a transitory phenomenon in subacute bacterial endocarditis and the development of this disease in patients with the *established* rhythmic disorder.

It is worthy of emphasis that no cases of auricular fibrillation were encountered under the age of forty years without signs of active rheu-

matic inflammation. As a matter of fact, the only case of fibrillation in rheumatic heart disease under forty years *without* activity, which we have studied,[28] was one in which bacterial endocarditis developed.

From the point of view of rhythm no significant relationship has been found to exist between the presence of any one or more associated lesions and active rheumatic carditis. One associated lesion appeared to bear a relationship to the rhythm, namely organic disease of the tricuspid valve; it is interesting that of 8 cases with tricuspid involvement which were studied histologically, seven were active.

Mural thrombosis in the material studied was confined to the auricles. It was encountered most often in the fibrillators with severe mitral stenosis and active carditis. Weiss and Davis,[44] in a study based on an analysis of necropsy protocols of 164 patients dying from rheumatic heart disease, reported organized mural thrombi in 30 cases. Of the 25 in their group in which the rhythm was determined, 22 showed auricular fibrillation. Using a combination of clinical and some pathological criteria, they stated that activity was present in only 18 per cent of their cases with auricular thrombi contrasting with activity of 47 per cent of their entire series of rheumatic hearts. The discrepancy between their results and the analysis presented here may be accounted for by the fact that their pathological data were taken from necropsy protocols and may not have been so comprehensive as the present study from this standpoint.

SUMMARY AND CONCLUSIONS

An analysis based on the study of 119 consecutive rheumatic hearts obtained at necropsy has been correlated with the cardiac rhythm. Correlations have been made with the grade of mitral valvular defect, age, presence of rheumatic inflammation in the heart and blood vessels, associated cardiac lesions, auricular thrombosis, and the mode of death.

It is shown that the occurrence of auricular fibrillation bears no relationship to the grade of mitral stenosis. Stenosis or organic insufficiency of the mitral valve is necessary for the development of *persistent* auricular fibrillation (not the transitory form) in rheumatic heart disease.

Auricular fibrillation in rheumatic heart disease is encountered with greater frequency in persons past middle life.

Auricular fibrillation is a usual manifestation of rheumatic activity in the presence of rheumatic structural cardiac lesions in individuals under forty years of age dying in congestive heart failure.

Significant organic disease of the tricuspid valve associated with mitral valvular disease is found more frequently among patients with auricular fibrillation than in those with sinus rhythm.

Auricular thrombosis in rheumatic heart disease is encountered most frequently in the hearts of individuals with auricular fibrillation, severe mitral stenosis and evidence of active rheumatic inflammation.

The trends seen in the data are discussed in relation to the etiology of the abnormal rhythm in rheumatic cardiac patients and in relation to clinical dicta concerning the relative immunity of certain types of rheumatic cardiac patients to the development of subacute bacterial endocarditis.

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THE HEARTS OF RICKSHA PULLERS

A Study of the Effect of Chronic Exertion on the Cardiovascular System*

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INTRODUCTION

OUR interest in the effect of prolonged physical exertion on the human cardiovascular system was aroused in 1930, when one of us (C.L.T.), in the course of routine physical examinations, found a markedly enlarged heart in an otherwise healthy ricksha puller employed in one of the departments of the College. This led to the study herein reported.

That physical exercise has an effect on the cardiovascular system has been realized for a great many years, but as to precisely what this effect is, opinions even today are divided. As early as 1628 Harvey[1] in his *Anatomical Studies on the Motion of the Heart and Blood* stated: "So all animals, man included, that have a stronger and more sturdy frame, with large, brawny limbs some distance from the heart, have a more thick, powerful, and muscular heart, as is obvious and necessary. On the contrary, those whose structure is more slender and soft have a more flaccid heart, less massive and weaker, with few or no fibers internally" (referring to the chordae tendineae and papillary muscles). Since the time of Harvey a mass of literature concerning the effect of exercise on the hearts of animals and of men has appeared. For a fairly complete bibliography the reader is referred to *Chronic Effects of Exercise* by Steinhaus[2] and to *The Physiology of Muscular Exercise* by Bainbridge and others.[3]

All data derived from studies of animals show that prolonged exertion produces cardiac hypertrophy. Animals in the wild state are known to possess relatively larger heart weight to body weight ratios than their domesticated relatives. The heart of the wild hare, for instance, is three times as heavy, relative to body weight, as that of the tame rabbit. Birds that fly great distances have much larger hearts in comparison with birds that lead a quiet life. Herrmann[4] demonstrated that heart weight to body weight ratios in racing greyhounds are considerably greater than the figures usually given for dogs. He weighed the hearts of ten thoroughbred greyhounds and found an average of 13.8 grams of heart

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per kilogram of body weight, which is considerably above the average of 7.98 for 200 normal mongrels. While the maximum ratio of the 200 mongrels was 9.98, the most successful runner among his greyhounds had a ratio of 17.3. From studies of the heart weight to body weight ratios of a large number of various animals, both young and full grown, Herrmann concludes that there is some fundamental relationship between the activity of individual mammals and their heart weight, body weight ratio, and that the more sluggish the animal, the smaller is the ratio. Even young greyhounds who have been confined to small kennels have relatively large hearts.[5]

In experimentally controlled studies on animals, Külbs[6] in 1906, Grober[7] in 1908, and Thörner[8] in 1930 all showed that the heart weight to body weight ratios of dogs exercised by running were markedly greater than those of their litter mates who received no exercise. Secher[9] in 1923 first demonstrated that cardiac hypertrophy experimentally produced by exercise would regress after adequate rest. Twenty-two rats were given daily running exercise for about sixty days, after which all were retired to inactivity. Small groups were then killed at intervals up to seventy-five days. In those killed immediately the heart weight constituted 5 to 6 per cent of the body weight. This percentage decreased until the forty-eighth day, when it reached the normal value of 3.3 to 3.5 per cent. Secher's findings were confirmed and extended by Steinhaus and his coworkers[10, 11] who studied the effects of running and swimming on the hearts of growing dogs. Four litters consisting of three dogs each were used. One was exercised by running, a second by swimming, while a third served as a control. All the dogs were permitted to play for a brief period twice a day in the open yard. Roentgenograms were secured biweekly throughout the observation, which lasted one and one-half years in most cases. The results were checked by post-mortem findings. The roentgenograms showed that strenuous exercise led to enlargement of heart, beyond that which was accounted for by the growth curve, within three to five weeks after the beginning of exercise. Whenever exercise was discontinued, there was a regression of the heart area in relation to the body weight curve. Autopsy revealed that exercise induced true work hypertrophy of the heart involving both ventricles, with a slight excess in favor of the left side. The enlargement was more marked in swimmers than in runners. There was no indication of comparable hypertrophy of the skeletal musculature of the limbs.

In regard to the effects of exercise on the human cardiovascular system, published findings are not so consistent as those for experimental animals. In explanation Steinhaus[2] mentions two probable factors: first, the shadow of the heart in man fuses at its lower border with that of the diaphragm; and second, conclusions have been drawn from comparisons of athletes' hearts with a large variety of so-called normal

standards. Two other considerations may be mentioned. First, it is very rare to obtain necropsies of vigorous athletes who meet an accidental death. Second, slight to even moderate hypertrophy may occur during life, but not be particularly obvious even on roentgen-ray examination unless dilatation is also present. As to the immediate effects of strenuous exercise on the size of the heart, Gordon, Levine, and Wilmaers[12] showed it to be reduced immediately upon cessation of exertion, probably because of sudden diminution of venous return to the heart.

There are in general three schools of opinion in regard to the chronic effects of exercise on the cardiovascular system. First, Gordon, Rautmann, and others[12, 13, 14, 15] hold that the heart size of heavy workers and athletes in general falls within the range for normal individuals of the same size and age. Deutsch and Kauf,[16] who examined several thousand athletes at the Vienna heart station and 32 athletes at the 1928 Amsterdam Olympic Games,[17] hold that the heart shadows of trained athletes average larger than those of similarly built ordinary individuals. According to them enlargement is most noticeable in those long engaged in endurance sports, such as oarsmen, skiers, and cyclists. They interpret this enlargement as dilatation associated with, or brought on by, vagotonia in athletes, since the enlargement usually subsides (though never completely) after several weeks or months of rest, and since bradycardia is such a common finding in athletes.[18] Herxheimer[19] represents the third group who hold that strenuous exercise produces true hypertrophy of the heart. He studied 171 participants in the German games of 1922, 12 professional six-day bicycle racers, and 249 Olympic athletes at Amsterdam in 1928. Eimer's[20] investigation of 300 athletes led him in the same direction. Herxheimer[21] presented the theory that exercises of strength or speed induce hypertrophy of skeletal muscles and only to a small extent of the heart muscle, whereas exercises of endurance cause cardiac hypertrophy without much effect on skeletal muscles. Ackermann[22] measured the hearts of oarsmen before and after a season of training. About half, mostly the younger men, showed definite enlargement at the end of the season.

TWO CASE REPORTS

The following cases are reported as of special interest to the problem.

CASE A.—(No. 43 of the tables). A healthy Chinese male employee of forty-five years, came for routine examination in April, 1930, with negative past and present histories. No cardiovascular or other complaints. Had been pulling a ricksha for about seven years, with an average of about four hours' actual running per day. Well developed and fairly well nourished. The only positive findings were moderate cardiac enlargement to the left and a slow heart rate, 48 per minute. Heart sounds of good quality. No murmurs. No detectable arteriosclerosis. No edema. Blood pressure 89 mm. Hg systolic and 62 mm. diastolic. Urine normal. Blood Wassermann reaction negative. A teleroentgenogram of the heart

(Fig. 1) showed a cardiac area on the frontal plane of 151.6 sq. cm., 47 sq. cm. above the estimated normal value for his height and weight. The cardiothoracic ratio of Danzer was 0.56. Although the man had no symptoms or signs pointing to cardiac insufficiency, it was thought that he should give up ricksha pulling. He was consequently transferred to an indoor occupation which necessitated no significant physical activity.

Further examination in April, 1933, three years after cessation of ricksha pulling, showed that the individual was in good physical condition. His heart was still enlarged to the left, though it appeared to be smaller than it had been three years before. The teleroentgenogram (Fig. 2) taken with the same technic showed a frontal heart area of 127.7 sq. cm., 23 sq. cm. oversized, but smaller than in 1930 by about 24 sq. cm. From the roentgenographic appearance, although the heart as a whole was reduced in size, the decrease involved chiefly the left ventricle. Electrocardiograms taken in 1930 and in 1933 revealed nothing remarkable.

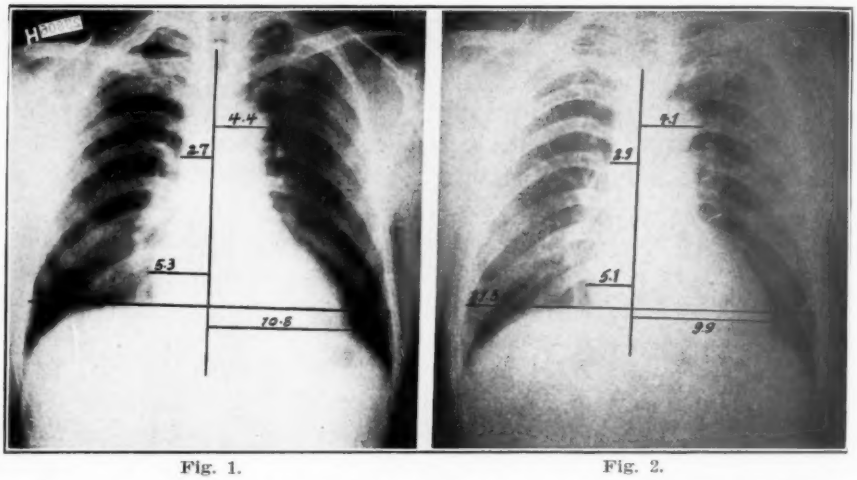

Fig. 1. Fig. 2.

Fig. 1.—Case 43*a*. Ricksha puller for seven years. April 13, 1930. Estimated cardiac area 104.65 sq. cm. Measured area 151.60 sq. cm. Heart oversize 47 sq. cm., or 45 per cent. Cardiothoracic ratio 0.56.

Fig. 2.—Case 43*b*. April 25, 1933, after three years of inactive occupation. Estimated cardiac area 104.84 sq. cm. Measured area 127.70 sq. cm. Heart oversize 22.86 sq. cm., or 22 per cent. Cardiothoracic ratio 0.54.

CASE B.—(Hosp. No. 40,272, not included in the group studied). A Chinese man, aged forty-seven years, admitted to the Surgical Service for anal fistula of twenty-nine years' duration. No complaint, except for the local condition. No symptom referable to the pulmonary or cardiovascular system. Venereal exposure denied; no intravenous medication. X-ray examination of the chest for tuberculosis revealed no evidence of tuberculosis, but a moderately enlarged heart, involving especially the left ventricle, both in frontal view and in left anterior oblique view, and marked enlargement or bulging of the ascending portion of the aortic arch (Fig. 3). Estimated cardiac area 98.94 sq. cm. and measured area 133.90 sq. cm., an increase of 35 sq. cm. Cardio-thoracic ratio 0.59. Diameter of the aortic shadow 8.2 cm.

Examination by the medical consultant showed no dyspnea or cyanosis. Faint pulsation in the right third interspace, but no thrill felt. Precordial impulse felt in the fifth and sixth intercostal spaces, 3 cm. beyond the midclavicular line. There was retromanubrial dullness and also dullness extending about 4 cm. to the right

of the midsternum in the second, third, and fourth intercostal spaces. Heart sounds of good quality; no accentuation or change in the quality of the aortic second sound. No murmur. Heart rate about 57, rhythm regular. Blood pressure 128 mm. Hg systolic and 72 mm. diastolic. No evidence of peripheral arteriosclerosis; no congestion of any viscera; no peripheral edema. No anemia or polycythemia. Urine normal. Ocular fundi showed slightly tortuous veins, normal in size; arteries apparently slightly narrower than usual; mild Gunn's crossing signs. These findings impressed the examiner as suggesting early primary hypertension. Both blood Wassermann and Kahn reactions negative on three occasions, about a month apart. Spinal fluid entirely normal, with flat colloidal gold and gum mastic curves and negative Wassermann reaction. Electrocardiogram showed sino-auricular rhythm, rate 57, auriculoventricular conduction time 0.21 second.

On inquiry it was found that the patient had been an active ricksha puller for eighteen years, with an average of about four hours' actual running per day. How-

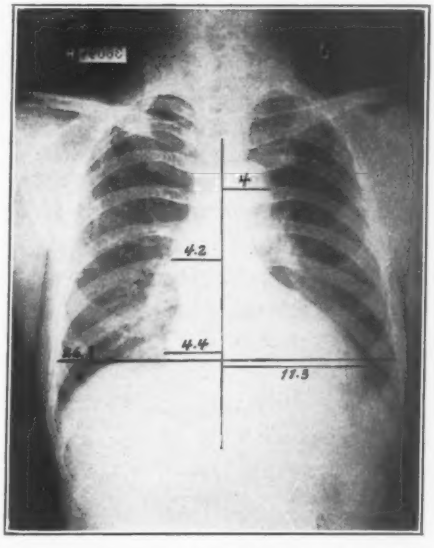

Fig. 3.—Case B (see case reports; not in the tables). Ricksha puller for eighteen years. Estimated cardiac area 98.94 sq. cm. Measured area 133.90 sq. cm. Heart oversize 35 sq. cm., or 35 per cent. Cardiothoracic ratio 0.59. Note the bulging of the ascending portion of the aortic arch.

ever, he insisted that he had always been in excellent health except for the anal fistula. Although it is possible that this patient may have syphilitic cardiovascular disease, it is extremely unlikely. It seems that the aortic dilatation and cardiac enlargement may well be the result of the patient's life as a ricksha puller.

MATERIAL AND METHODS

In an effort to throw further light on the problem of the effects of prolonged exertion on the heart, we have studied 46 ricksha pullers (all male). For the sake of those who have not seen a ricksha in use, it may be stated that it is a rather light narrow carriage, with two wire-spoked, rubber-tired wheels; a seat is mounted on leafed springs over the axle. The wheels are ball-bearing. Two shafts connected at the front by a

cross-piece extend forward. It is pulled by an individual who stands between the shafts. No effort is required to hold up the shaft, because once raised the rider and seat are balanced over the axle. On level ground little energy is needed to maintain the pull on the ricksha, and the energy is chiefly consumed in running, which at one stretch may vary from a short distance to one or two miles.

Most of the group of ricksha pullers studied are privately employed by members of the staff of the College. All the subjects had been ricksha pullers for at least one year. Their living conditions are fairly good. They usually have adequate rest between periods of activity. All of them were physically healthy and free from cardiovascular and other systemic disease. None of them was anemic. There was no evidence of nephritis in any. None of the group had any undue dyspnea after moderate speed and duration of pulling. There was no cyanosis or edema in any of them. None showed a cardiac diastolic murmur. The Wassermann test was not performed as a routine; some of the subjects had a previous record of a negative test. One of them (No. 33) had a positive blood Wassermann with no manifest syphilitic lesion. In short, all were athletic and apparently healthy individuals.

Groups of four or more subjects were examined by two of us (C.L.T. and C.W.B.) in the afternoon. All were given adequate rest before the examination. Quite a number came rather reluctantly, and a few were excited and almost refused the examination. Such an emotional upset may account for the tachycardia and slight elevation of blood pressure (which usually disappeared after reassurance) noted in a number of cases. The physical examination was carried out before roentgenologic and electrocardiographic studies were made. Particular attention was paid to the cardiovascular system, although it must be stated that only a brief period was available for physical examination in order that all studies could be completed in one afternoon. During the physical examination the heart was considered "not enlarged" when the outermost point at which a distinct cardiac impulse could be felt was on or within the midclavicular line, or the outermost point of the cardiac dullness on light percussion was on or within the same line. The heart was considered "enlarged" when the cardiac impulse could be distinctly felt beyond the midclavicular line, or if this was not palpable, when the relative cardiac dullness extended beyond that line. Determination of the cardiac size by physical examination is subject to error from at least three factors, aside from the error due to haste in the examination or to poor technic. When the heart is hyperactive, as in excitement and apprehension, the vibration of the precordial region may be so widespread that the heart may be considered enlarged, while actually it is not. Even when the left border of the heart is beyond the midclavicular line, decision as to the size of the heart is fraught with insecurity if the measured cardiac area in the teleroentgenogram is not above the upper

limit of the estimated normal. On the other hand, when enlargement of the heart is general or more right-sided, the left border may be within the midclavicular line, while the heart is actually oversize.

Blood pressure was taken by the auscultatory method, and the beginning of the fourth phase was taken as the diastolic level. The peripheral arteries were considered "thickened" when the wall of either the brachial or radial artery or both, emptied of its blood content, could be readily felt by the palpating finger. Complete urinalysis was done. The finding of a trace of albumin and leucocytes in the sediment could usually be traced to chronic gonococcal urethritis.

The final decision as to whether the heart was enlarged or not was based on the results of radiological study. At the laboratory the subject was first examined under the fluoroscope in various positions. Particular attention was paid to the heart and the aortic arch. A frontal teleroentgenogram with the subject at a distance of two meters from the target was then taken. An additional film was taken with the subject in the left anterior oblique position, facing the film at an angle of 45 degrees. In the latter position the two ventricles can be better visualized and their relative size determined more accurately after the method originally suggested by Fray.[23] The cardiac area was measured with a planimeter. The difference between the measured area and the estimated normal area was recorded and then expressed in percentage. The estimation of cardiac area was done according to the method of Hodges and Eyster.[24] In addition the cardiothoracic ratio of Danzer[25] was calculated.

With the string standardized so that a current of one millivolt gave a deflection of one centimeter on the record, Leads I, II, and III of the electrocardiogram were taken from each subject in the recumbent position. The subjects were not in a basal condition. The T-wave was considered tall in a lead when its height was above 5 mm. The presence of right or left "axis deviation" was determined from Leads I and III. The longest P-R interval was measured, usually in Lead II. The R-R interval and the Q-T interval were determined by taking the average values of four cycles. The relative duration of electrical systole as expressed in the formula, K equals the Q-T interval divided by the square root of the R-R interval, was then calculated.[26]

RESULTS

Table I summarizes the results of the physical findings in these 46 ricksha pullers. Their mean age was thirty-three years. The period during which they had been engaged in their occupation averaged about eight years. The extremes were one year and twenty-five years. Most of the subjects actually pulled from two to four hours per day (mean, 3.3 hours). Twenty-one of the 46 subjects (45 per cent) revealed evidence of cardiac enlargement. Thickening of brachial or radial artery

TABLE I

PHYSICAL FINDINGS IN 46 RICKSHA PULLERS (All Male)

NO.	AGE	ACTIVITY	ACTUAL PULLING PER DAY	HEART SIZE	PERIPHERAL ARTERIES	BLOOD PRESSURE	CARDIAC MURMURS	URINE
	Years	*Years*	*Hours*			*mm. Hg*		
1	19	2	4	Not enlarged	Soft	100/68	Systolic apical	Normal
2	21	6	3	Not enlarged	Soft	90/56	None	Normal
3*	22	2	3	Not enlarged	Soft	92/64	None	Normal
4	22	2	3	Not enlarged	Thickened	120/82	None	Normal
5	22	3	2	Enlarged	Soft	106/72	None	Normal
6	24	3	4	Not enlarged	Soft	116/78	None	Normal
7	24	1	1	Not enlarged	Soft	106/70	None	Normal
8	25	2	3	Enlarged	Soft	100/60	None	Trace albumin, many W.B.C.
9*	26	3	4	Not enlarged	Soft	116/46	Systolic apical and basal	Normal
10	27	7	4	Enlarged	Soft	134/90	None	Normal
11*	27	2	3	Enlarged	Soft	128/80	Systolic basal	Normal
12	28	5	3	Not enlarged	Thickened	102/80	None	Trace albumin, many W.B.C.
13*	29	15	3	Not enlarged	Thickened	130/90	None	Normal
14*	29	8	2	Enlarged	Soft	124/68	None	Normal
15*	30	7	3	Not enlarged	Soft	104/62	None	Normal
16	30	7	4	Enlarged	Soft	96/66	None	Normal
17	30	12	4	Not enlarged	Soft	112/76	None	Trace albumin, many W.B.C.
18*	30	4	2	Enlarged	Soft	116/76	None	Normal
19*	30	9	3	Enlarged	Thickened	120/74	Systolic apical	Normal
20*	31	2	6	Not enlarged	Soft	134/78	Systolic apical and basal	Normal
21	31	2	3	Not enlarged	Soft	108/80	None	Normal
22*	32	10	4	Enlarged	Soft	126/78	None	Normal
23*	33	5	3	Not enlarged	Soft	112/84	None	Normal
24a	31	10	2	Enlarged	Thickened	118/82	None	Normal
24b	33	12	2	Enlarged	Thickened	110/68	None	Normal
25	35	10	2	Not enlarged	Thickened	126/80	None	Normal

*Cases so marked have cardiac areas 15 per cent or more above the estimated area in teleroentgenograms. In the calculation of mean values, 24a, 32a, 43b, and 45a were excluded. The records of 43b were obtained after three years of an inactive occupation.

TABLE I—CONT'D

NO.	AGE	ACTIVITY	ACTUAL PULLING PER DAY	HEART SIZE	PERIPHERAL ARTERIES	BLOOD PRESSURE	CARDIAC MURMURS	URINE
	Years	*Years*	*Hours*			*mm. Hg*		
26*	35	6	4	Enlarged	Thickened	126/88	None	Normal
27*	35	4	4	Not enlarged	Soft	110/80	None	Normal
28	36	7	3	Enlarged	Thickened	134/84	None	Normal
29	36	10	3	Not enlarged	Soft	116/80	None	Normal
30	36	15	2	Enlarged	Soft	134/84	Systolic basal	Normal
31*	36	12	6	Enlarged	Soft	120/86	None	Normal
32a	35	4	5	Not enlarged	Thickened	108/72	None	Normal
32b	37	6	5	Not enlarged	Thickened	114/76	None	Normal
33	37	6	4	Not enlarged	Soft	108/72	None	Normal
34	38	20	2	Enlarged	Sclerotic and tortuous	108/78	Systolic apical	Normal
35	39	13	3	Enlarged	Soft	128/72	Systolic apical	Normal
36	39	14	2	Not enlarged	Soft	122/80	Systolic basal	Normal
37	40	25	3	Not enlarged	Soft	104/74	None	Normal
38	40	20	3	Not enlarged	Soft	104/70	None	Normal
39*	40	18	3	Not enlarged	Sclerotic	120/80	None	Trace albumin, many W.B.C.
40*	41	10	3	Not enlarged	Soft	108/78	None	Normal
41*	42	10	3	Enlarged	Thickened	120/80	None	Trace albumin, few W.B.C.
42	44	7	3	Enlarged	Sclerotic	112/80	Systolic apical	Trace albumin, occasional granular casts
43a*	45	7	4	Enlarged	Soft	80/48	None	Normal
43b*	48	–	–	Enlarged	Soft	88/60	None	Normal
44*	47	5	4	Enlarged	Sclerotic	104/70	Systolic apical and basal	Normal
45a	47	15	5	Not enlarged	Soft	96/64	None	Normal
45b	49	17	5	Not enlarged	Soft	106/76	None	Normal
46*	49	18	6	Enlarged	Thickened	116/76	None	Normal
Mean	33	8	3.3			114/75		

was noted in 17 individuals; the brachial artery was sclerotic and tortuous in one man who was thirty-four years of age. These findings are suggestive of early arteriosclerosis. It is our impression that there is a

TABLE II

TELEOROENTGENOGRAPHIC FINDINGS IN 46 RICKSHA PULLERS

NO.	HEIGHT	WEIGHT	ESTIMATED CARDIAC AREA	MEASURED CARDIAC AREA	DIFFERENCE	CARDIO-THORACIC RATIO	AORTIC DIAMETER	ROENTGENOLOGICAL IMPRESSION
	cm.	*kg.*	*sq. cm.*	*sq. cm.*	*per cent*		*cm.*	
1	157.0	47.0	88.77	84.50	− 5	12.0:24.2 0.50	5.2	Normal heart
2	166.0	54.0	97.24	96.20	− 1	12.7:23.5 0.54	4.4	Normal heart. Slight left ventricular enlargement
3*	171.0	56.5	104.18	125.70	+21	13.9:27.6 0.50	6.5	General cardiac enlargement
4	174.0	58.7	107.54	114.40	+ 6	13.2:26.0 0.51	7.0	Normal heart. Aortic shadow slightly widened
5	169.0	60.5	103.80	112.40	+ 8	13.3:25.5 0.52	5.8	Normal heart
6	175.5	50.5	106.05	110.30	+ 4	13.3:25.4 0.52	5.7	Normal heart. Slight left ventricular enlargement
7	168.0	57.5	102.34	115.20	+13	12.9:27.5 0.47	5.6	Slight cardiac enlargement
8	154.5	51.0	88.77	93.80	+ 7	13.4:23.6 0.57	5.7	Left ventricular enlargement
9*	165.5	58.5	100.07	116.20	+16	13.7:26.0 0.53	6.5	General cardiac enlargement
10	164.0	60.4	98.41	111.00	+13	13.9:24.5 0.56	6.5	General cardiac enlargement

TABLE II—CONT'D

NO.	HEIGHT	WEIGHT	ESTIMATED CARDIAC AREA	MEASURED CARDIAC AREA	DIFFERENCE	CARDIO-THORACIC RATIO	AORTIC DIAMETER	ROENTGENOLOGICAL IMPRESSION
	cm.	*kg.*	*sq. cm.*	*sq. cm.*	*per cent*		*cm.*	
11*	164.0	52.2	96.63	128.80	+35	13.5:25.0 0.54	5.8	Left ventricular cardiac enlargement
12	160.0	51.3	92.84	90.50	− 2	11.2:27.0 0.41	5.8	Normal heart
13*	171.5	63.3	106.92	126.20	+18	14.4:26.7 0.53	8.0	General cardiac enlargement. Aortic arch widened and slightly tortuous
14*	168.0	52.4	100.18	136.30	+36	13.1:24.0 0.54	5.8	General cardiac enlargement
15*	172.0	60.0	106.24	122.00	+15	14.6:25.0 0.58	5.6	Left ventricular cardiac enlargement
16	168.0	53.0	100.38	97.75	− 3	13.0:26.0 0.50	5.1	Normal heart
17	180.0	61.3	113.64	92.70	−10	12.4:26.5 0.47	6.0	Normal heart. Aortic arch elongated
18*	166.0	58.0	100.34	124.20	+24	13.5:29.0 0.47	5.7	General cardiac enlargement
19*	166.0	53.0	98.64	115.00	+16	13.7:25.5 0.54	6.1	Left ventricular cardiac enlargement
20*	160.0	54.8	94.03	123.40	+31	13.5:25.6 0.53	6.4	General cardiac enlargement

TABLE II—CONT'D

NO.	HEIGHT	WEIGHT	ESTIMATED CARDIAC AREA	MEASURED CARDIAC AREA	DIFFERENCE	CARDIO-THORACIC RATIO	AORTIC DIAMETER	ROENTGENOLOGICAL IMPRESSION
	cm.	*kg.*	*sq. cm.*	*sq. cm.*	*per cent*		*cm.*	
21	169.0	53.7	101.50	103.80	+ 2	12.7:24.8 0.51	5.7	Normal heart
22*	166.0	56.5	99.83	136.90	+37	14.6:25.0 0.58	7.1	Left ventricular cardiac enlargement
23*	160.4	62.6	97.03	144.60	+49	15.0:25.0 0.60	7.0	Marked general cardiac enlargement. Left ventricle prominent
24a	190.0	75.0	127.00	112.00	−13	13.5:26.6 0.51	5.7	Normal heart
24b	192.0	76.0	129.25	123.35	− 5	13.8:26.7 0.52	5.5	Normal heart
25	177.0	63.8	111.88	119.10	+ 6	14.4:28.8 0.50	7.5	Normal heart. Aortic shadow widened
26*	156.0	56.2	91.03	137.30	+51	14.4:27.8 0.52	7.6	Marked general cardiac enlargement. Aortic shadow widened
27*	167.0	65.2	103.66	123.60	+19	14.5:28.5 0.50	6.8	General cardiac enlargement
28	172.0	71.2	111.05	125.40	+14	14.5:29.0 0.50	6.8	General cardiac enlargement
29	182.0	63.0	116.06	111.70	− 4	13.6:24.0 0.57	5.9	Normal heart. Left ventricle prominent

TABLE II—CONT'D

NO.	HEIGHT	WEIGHT	ESTIMATED CARDIAC AREA	MEASURED CARDIAC AREA	DIFFERENCE	CARDIO-THORACIC RATIO	AORTIC DIAMETER	ROENTGENOLOGICAL IMPRESSION
	cm.	*kg.*	*sq. cm.*	*sq. cm.*	*per cent*		*cm.*	
30	157.0	55.2	91.55	98.50	+ 8	13.3:25.5 0.52	5.5	Normal heart
31*	168.0	61.0	103.10	120.80	+17	13.3:28.0 0.48	5.5	Left ventricular cardiac enlargement
32a	162.0	54.0	95.57	103.00	+ 7	12.8:26.5 0.48	5.9	Normal heart
32b	162.0	54.0	95.57	91.85	- 4	12.2:29.5 0.42	5.4	Normal heart
33	174.5	57.6	108.60	113.65	+ 4	13.5:29.5 0.46	5.3	Normal heart
34	171.3	66.0	107.67	113.60	+ 6	13.4:26.5 0.51	6.4	Normal heart. Aortic arch tortuous
35	168.5	57.5	102.34	115.20	+13	12.9:27.5 0.47	5.6	Left ventricular cardiac enlargement
36	169.5	61.3	104.50	103.90	- 1	11.7:29.0 0.40	5.5	Normal heart
37	168.5	53.3	100.91	88.80	-12	12.2:24.0 0.51	5.8	Normal heart
38	172.0	60.0	106.14	106.10	0	13.2:26.5 0.50	7.0	Normal heart. Aortic arch tortuous and elongated

TABLE II—CONT'D

NO.	HEIGHT	WEIGHT	ESTIMATED CARDIAC AREA	MEASURED CARDIAC AREA	DIFFERENCE	CARDIO-THORACIC RATIO	AORTIC DIAMETER	ROENTGENOLOGICAL IMPRESSION
	cm.	*kg.*	*sq. cm.*	*sq. cm.*	*per cent*		*cm.*	
39*	174.5	63.0	109.43	129.30	+18	13.3:28.0 0.48	7.9	General cardiac enlargement. Aortic arch prominent and elongated
40*	164.5	57.3	98.80	120.80	+22	15.0:25.0 0.60	6.3	Left ventricular cardiac enlargement
41*	175.0	58.0	108.14	141.50	+31	15.4:27.0 0.57	6.7	General cardiac enlargement
42	156.0	41.7	86.10	90.00	+ 5	11.1:23.2 0.47	5.4	Normal heart. Aortic arch tortuous
43a*	169.0	63.0	104.65	151.60	+45	16.1:28.3 0.56	7.1	Marked cardiac enlargement, especially of left ventricle
43b*	170.0	61.0	104.84	127.70	+22	15.0:27.5 0.54	7.0	Heart still enlarged, but smaller. Reduction in left ventricle chiefly
44*	160.5	52.7	93.74	116.80	+25	13.9:26.0 0.52	6.1	Left ventricular cardiac enlargement
45a	178.0	63.4	112.65	109.00	- 3	13.2:26.2 0.50	6.4	Normal heart
45b	178.0	63.5	112.65	106.30	- 6	13.7:29.7 0.47	5.7	Normal heart. Aortic arch elongated
46*	152.0	41.0	82.38	102.33	+24	13.6:25.8 0.49	6.5	Left ventricular cardiac enlargement
Mean	167.8	57.6	103.5 ± 2.6	114.6 ± 2.3	+13.2 ± 2.3	0.51	6.1	

*Cases so marked have cardiac areas 15 per cent or more above the estimated area.
In the calculation of the mean values, 24a, 32a, 43b, and 45a were excluded.

higher incidence of the thickening of the peripheral arteries in this group than is usually found in physical examinations of healthy individuals of the same age periods.

The mean blood pressure was 114 mm. Hg systolic and 75 mm. diastolic; the mean pulse pressure was 39 mm. The pressure tended to be high in a few cases. Blood pressures of 130 mm. systolic and 90 mm. diastolic in a young man of twenty-nine years (Case 13) and of 134 mm. systolic and 84 mm. diastolic in two subjects thirty-six years old (Cases 28 and 30) are not usual among the Northern Chinese. The mean values are very slightly higher than the mean and median systolic pressure of 107 and diastolic pressure of 70 in a series of 342 healthy, active Northern Chinese males of the age period of thirty to thirty-nine years.[27]

The roentgenological findings are summarized in Table II. The results of the fluoroscopic examination are incorporated in the column, "General impression," which represents the opinion of one of us, the roentgenologist (C.K.H.). In evaluating the measured frontal cardiac areas in teleroentgenograms, the tables of Hodges and Eyster[24] for the calculation of the expected normal area have been used. These tables are based on a study of 70 normal Americans. Whether they apply strictly to Chinese subjects has not been definitely settled, but our measurements of the cardiac area of 140 normal, healthy, adult Chinese

TABLE III

PERCENTAGE DEVIATION FROM CARDIAC AREA ESTIMATED FROM HEIGHT AND WEIGHT

PERCENTAGE DEVIATION FROM ESTIMATED CARDIAC AREA	NORMAL CHINESE MALES		RICKSHA PULLERS	
	NUMBER	PER CENT	NUMBER	PER CENT
−30 to −26	1	1.0	0	0
−25 to −16	8	6.0	0	0
−15 to − 6	55	39.0	3	6.5
	=	=	12	26.0
− 5 to + 4	56	40.0	=	=
	=	=	11	24.0
+ 5 to +14	17	12.0	=	=
	=	=	11	24.0
+15 to +24	3	2.0	=	=
+25 to +34	0	0	3	6.5
+35 to +44	0	0	3	6.5
+45 to +54	0	0	3	6.5
Total	140	100	46	100

males, mostly staff members and medical students of this institution, show that the mean cardiac area of normal Chinese males is 4.2 per cent (±0.68 standard error) smaller than that predicted from age, height, and weight. In Table III it will be seen that 79 per cent of normal Chinese males have measured cardiac area between −15 per cent and +4 per cent and only 12 per cent between +5 and +14 per cent. Thus the cardiac area of normal Chinese males tends to be undersized by about 4 per cent, when compared with predicted area calculated according to

Fig. 4. Fig. 5.

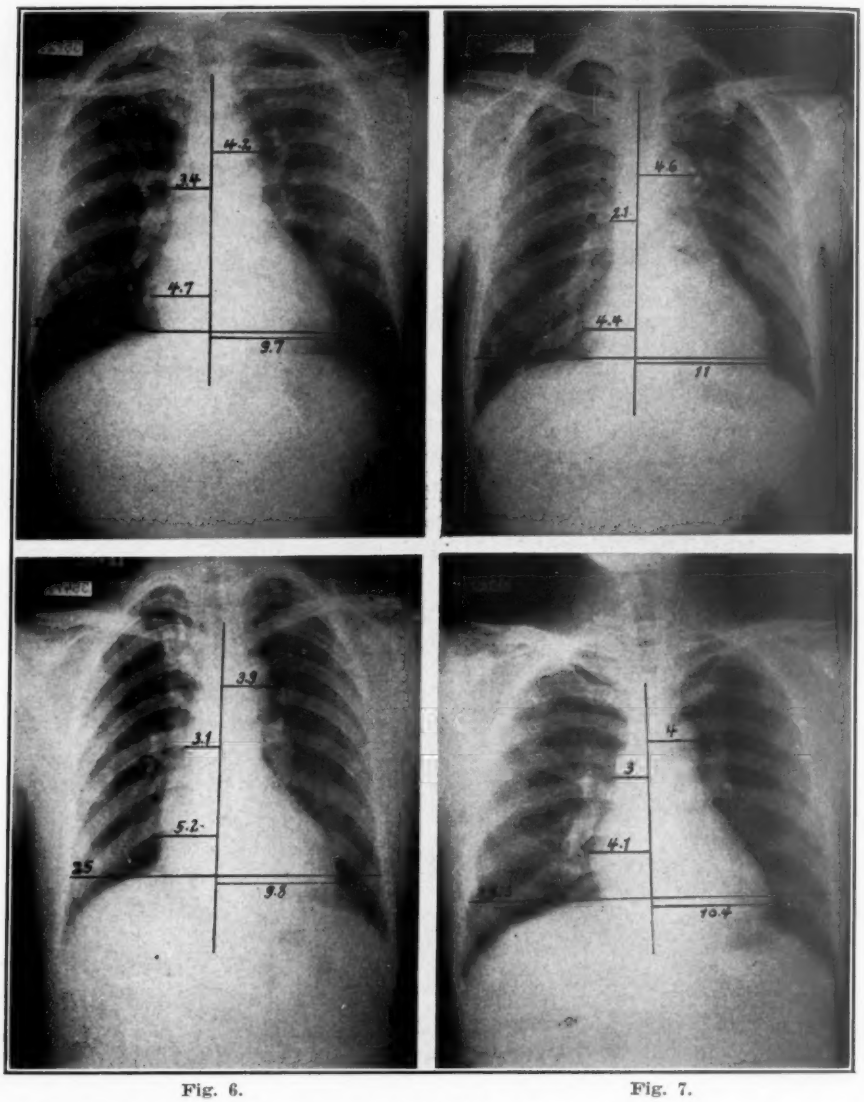

Fig. 6. Fig. 7.

Fig. 4.—Case 26. Ricksha puller for six years. Estimated cardiac area 91.03 sq. cm. Measured area 137.30 sq. cm. Heart oversize 46.27 sq. cm., or 51 per cent. Cardiothoracic ratio 0.52.

Fig. 5.—Case 41. Ricksha puller for ten years. Estimated cardiac area 108.14 sq. cm. Measured area 141.50 sq. cm. Heart oversize 33.36 sq. cm., or 31 per cent. Cardiothoracic ratio 0.57.

Fig. 6.—Case 23. Ricksha puller for five years. Estimated cardiac area 97.03 sq. cm. Measured area 144.60 sq. cm. Heart oversize 47.57 sq. cm., or 49 per cent. Cardiothoracic ratio 0.60.

Fig. 7.—Case 27. Ricksha puller for four years. Estimated cardiac area 103.66 sq. cm. Measured area 123.60 sq. cm. Heart oversize 19.94 sq. cm., or 19 per cent. Cardiothoracic ratio 0.50.

Hodges' method. These results seem to justify fully the use of the tables referred to.

In Cases 23, 32, and 45 there were two examinations done two years apart, and in Case 43 the first examination was done when the subject was engaged in ricksha pulling and the other after he had been in a sedentary occupation for three years. In the final calculation of the data the results of the more recent examination, when the subject had more than one, were included as representative, with the exception of Case 43, as the result of the later examination was considered to be affected by the three years' rest.

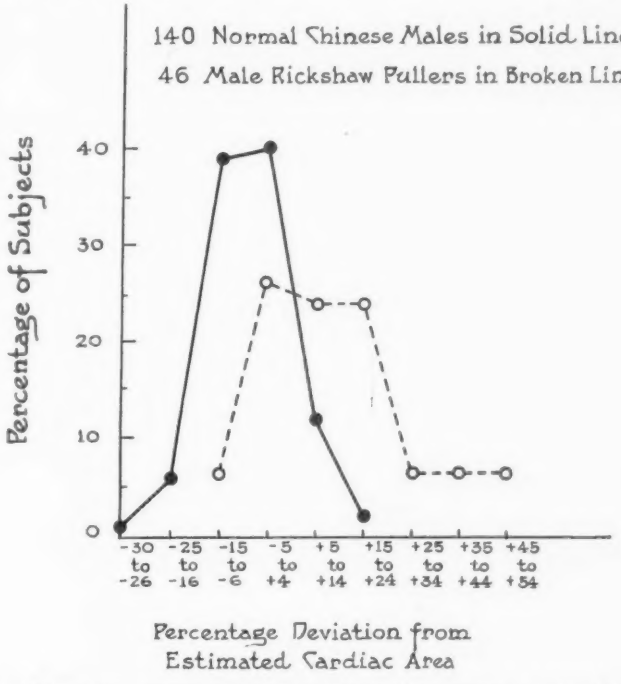

Fig. 8.—Distribution curves comparing the cardiac areas of 46 ricksha pullers (males) and those of 140 normal Chinese men. For each subject the difference between the measured area and the estimated area is expressed in per cent.

According to Hodges and Eyster, with an observed area 14 sq. cm. larger than the predicted area, the chances are ten to one that the heart is abnormally large. On this basis, which is also in accord with our clinical experience, we have considered a heart to be definitely enlarged when the observed area is 15 per cent or more above the predicted area, since we think percentage deviation is more significant than the difference in actual square centimeters. Of the 46 subjects, 20, or 43 per cent, had observed heart areas larger than the predicted area by 15 per cent or more.

Figs. 1, 2, 4, 5, 6, 7, 8 are examples of x-ray shadows of enlarged hearts.

We may compare our findings in ricksha pullers with the results in the group of 140 normal adult male Chinese by referring to Table III and Fig. 8. Statistically the data may be summarized as follows:

DEVIATION OF CARDIAC AREA	MEAN VALUE ± STANDARD ERROR
46 ricksha pullers	+ 13.2 ± 2.3 per cent
140 normal adult male Chinese	− 4.2 ± 0.68 per cent
Difference	17.4 ± 2.38

The results for the 46 ricksha pullers in comparison with the American standard are shown below:

Average measured cardiac area	114.6 ± 2.3 sq. cm.
Average estimated cardiac area	103.5 ± 2.6 sq. cm.
Difference	11.1 ± 3.5 sq. cm.

The differences, especially that between the mean deviation of the cardiac area of ricksha pullers and that of the cardiac area of normal Chinese, are clearly statistically significant.

In order to evaluate the cardiothoracic ratio of Danzer,[25] a study was made of 116 of the 140 telecardiograms of normal male Chinese. The resulting mean ratio is 0.485 ± 0.004 (standard error). It would seem safe to assume that a ratio of 0.52 or more indicates some degree of cardiac enlargement. In Tables II and III it is shown that the ratio is 0.52 or greater in 22 (48 per cent) of the 46 ricksha pullers. This slightly higher percentage of cardiac enlargement than was shown by the measured area is probably due to the fact that while cardiac enlargement is usually general in nature, there is a tendency to a preponderant enlargement of the left ventricle, as may be seen in Figs. 1, 2, 4, 5, 6, 7.

In summary, nearly half of the ricksha pullers examined showed demonstrable cardiac enlargement (43 to 48 per cent according to the criterion used). Conversely over half the subjects showed no evidence of enlargement beyond the normal limit.

Examination of the data fails to disclose any relation between the years of activity, (minimum, one year) and the occurrence of enlargement of the heart, which was present in four men who had pulled for only two or three years (Cases 3, 9, 11, and 20) and absent in eleven who had been in this occupation for ten or more years (Cases 17, 24, 25, 29, 30, 34, 35, 36, 37, 38, 45).

ACTIVITY	HEART NORMAL	HEART ENLARGED	TOTAL
1 to 4 years	7	6	13
5 to 9 years	8	7	15
10 or more years	11	7	18
Total	26	20	46

In addition to its size, the shape of the heart shadow of ricksha pullers needs brief mention. Although general cardiac enlargement was the usual finding, at least slight left ventricular enlargement was noted

in 15 instances, both among those that showed demonstrable total cardiac enlargement and among those that did not. The diameter of the aortic shadow measured 7 cm. or more in nine subjects. The aortic arch appeared to be elongated or tortuous, or both, in seven instances. Such findings are not usually encountered in healthy subjects of the same age period.

The electrocardiographic findings are not of great interest. The heart rate was not basal as the subjects were examined under the ordinary conditions in the laboratory. It may, therefore, be noteworthy that seven subjects had a rate below 60 beats per minute, and that the average rate was only 68. The electrical axis of the QRS complex lay within normal limits in 40 subjects; in one there was right axis deviation and in five left axis deviation. One striking feature is that in 16 cases the T deflection was tall in one or more leads.

The auriculoventricular conduction time was 0.20 second in eight individuals and beyond 0.20 second in four individuals; these values are usually associated with a slow sinus rhythm.

The average value for the constant K of the formula used for electrical systole[26] is 0.388 ± 0.0022 (standard error). This value may be compared to that for normal Chinese males[28] as follows:

116 normal Chinese males	0.374 ± 0.0012
46 ricksha pullers	0.388 ± 0.0022
Difference	0.014 ± 0.004

There is a slight but probably not significant difference.

DISCUSSION

Although the number of ricksha pullers examined is relatively small, the data presented seem to warrant certain conclusions.

In the first place, about 50 per cent of the subjects had hearts that were demonstrably enlarged. This in itself, we believe, is an important and significant finding. Although previous careful studies of animals and of athletes have shown that cardiac hypertrophy is a natural result of prolonged muscular exercise, clinicians have usually held to the dictum that an enlarged heart is a diseased heart.[29] None of the individuals studied had any other sign of disease than cardiac enlargement (and in some cases widening of the aorta), and all were actively engaged in an occupation calculated to bring out such signs. It must be admitted that we have no post-mortem examinations to report, and, therefore, final proof is lacking. It is, however, a fair conclusion, as far as the evidence goes, that the cardiac enlargement found is probably related to the physical activity of the subjects.

The physiological basis for cardiac hypertrophy in response to prolonged unusual exercise is clear. Studies have shown that the minute volume put out by the heart may be raised to 20 or more liters in severe

exercise, and that in highly trained men the increase in minute volume output of the heart is obtained to a much greater extent by increase in the stroke volume of the heart and, to a much smaller extent, by acceleration of the rate. In the case of De la Mar, a Marathon runner, it was shown by Bock, Van Caulaert, Dill, and others[30] that his stroke volume at rest was double that of untrained subjects and during work it rose to 200 c.c. Similar results have been reported by Hill and Lupton.[31]

Bainbridge et al.[3] point out the advantages of a powerful myocardium, with complete systolic emptying and but slight dilatation and tachycardia. He says, "Hence, for the making of an athlete, a large and muscular heart is just as much a physiological necessity as a highly developed muscular system, since, whatever the size of his muscles, a man's ability to perform muscular work is determined by the output of his heart."

The ricksha pullers examined must be considered to have been successful in their occupation, because they were not new at it and were selected by their employers from a large field of applicants. It must be noted here that the hypertrophy which we believe they showed may well not occur in all who endeavor to take up ricksha pulling.

Attention is called to the exact nature of the activity involved. It consists of running and pulling the ricksha, often for fair distances; but most important, this is done for a few hours a day, day after day for years, with few if any days of inactivity. There is no evidence to settle the point, but the suggestion may be made that running and other forms of extensive bodily motion may be more effective in producing cardiac changes than other forms of hard work. There can be no doubt that unintermitting daily activity for years would be more effective than intermittent or brief exercise. Even highly active athletes often have long intermissions in their periods of training.

In the second place, our results include evidence of widening of the aorta in some instances of relatively young men with no trace of syphilis. If this unusual finding in normal subjects has a physiological basis, the explanation can be found in the effect of the sustained increased blood pressure during exertion upon the elastic aortic wall.

Third, there arises the question whether such cardiac enlargement as was found is entirely physiological or not. In other words, is there such a disease as athletic heart?

As far as our results go, they give no indication for regarding the abnormal findings encountered as constituting or predisposing to disease. The men in whom cardiac enlargement was present had no evidence of the slightest heart failure and were holding their positions in competition with thousands of others. Many ricksha pullers continue in their occupation for long years, twenty and more years not being uncommon. One must also consider the men in our study who had been in their occupation for years without showing cardiac enlargement. They

also were successful. Possibly they should be regarded as being better adapted. Even this conclusion does not mean that the group with enlargement is, or will be, diseased, since it is merely a matter of relative fitness.

It is of course possible that, while the effects of prolonged exertion are purely physiological for the time being, they may accelerate the normal wear and tear of life. In that case they would not be direct but only contributory causes of death.

It is a common impression in China that the work of ricksha pullers is unduly hard, that damage is done to the heart and that the men cannot remain long in the occupation but die prematurely. The only reference in medical literature which we have found is in Chinese.[32] This is a report of physical examinations of 36 ricksha pullers. The author found the apex impulse of the heart beyond the nipple line in every case, and considered this to mean cardiac enlargement. Bradycardia was common. The findings were attributed to the ricksha pulling and interpreted as constituting disease. Valvular lesions and rupture of cerebral vessels were considered possible consequences. No x-ray or other laboratory examination was made. Our impression is that ricksha pulling is not in itself unduly hard and could not be compared to the work of stevedores, for example. On the other hand the life of public ricksha pullers is extremely difficult because, owing to their very small earnings, they cannot feed, clothe, and house themselves properly, and because they are compelled to expose themselves for long hours to all the inclement weather which the climate imposes. It does not appear that they are engaged in pulling their rickshas for long periods, because of severe competition for passengers. If their lives are short, exposure and privation are probably responsible.

SUMMARY

1. Forty-six healthy Chinese ricksha pullers were examined in a study of the effect of chronic exertion on the cardiovascular system. Physical, roentgenological, and electrocardiographic studies were carried out.

2. The mean age was thirty-three years. The mean duration of ricksha pulling was eight years, and the mean number of hours of actual running slightly over three per day.

3. Twenty-one (45 per cent) of the 46 ricksha pullers showed definite cardiac enlargement on physical examination which was always performed before radiographic examination.

4. The measured frontal cardiac area of the teleroentgenogram of the heart was 15 per cent or more above the area calculated according to the method of Hodges and Eyster in 20 individuals (43 per cent).

5. The mean deviation of measured cardiac area of 140 normal Chinese males from the calculated area in per cent was minus 4.2 ± 0.68 (stan-

dard error). The mean deviation of measured cardiac area of the 46 ricksha pullers from the calculated area in per cent was plus 13.2 ± 2.3. The difference between these two groups was 17.4 ± 2.38.

6. The cardiothoracic ratio of Danzer in telecardiograms was 0.52 or greater in 22 ricksha pullers (48 per cent). The mean ratio of the telecardiograms of 116 normal Chinese males was 0.485 ± 0.004.

7. Chronic exertion in the form of ricksha pulling caused cardiac enlargement in about 45 per cent of the subjects. No demonstrable enlargement was present in the remainder. This cardiac enlargement, probably chiefly due to hypertrophy, is considered to be a physiological response to rapid exertion carried on daily for a period of years. There is no indication that the enlargement constitutes or predisposes to disease.

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THE PATENCY OF THE SO-CALLED "ANATOMICALLY OPEN BUT FUNCTIONALLY CLOSED" FORAMEN OVALE*

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ZAHN[1] and Mönckeberg[2] indicate that under certain conditions the so-called "anatomically open but functionally closed" foramen ovale may become patent and lead to paradoxical embolism. Other reports in the literature add support to this contention, including the more recent publications of Beattie[3] and of French,[4] which give autopsy findings of emboli caught in the foramina ovale. It has been claimed that when the right auricular pressure exceeds the left auricular pressure, the functionally closed foramen becomes patent. Because this type of foramen ovale has not been universally recognized as a factor in the production of paradoxical embolism, the present study of the behavior of the foramen ovale under various differences in auricular pressures was undertaken.

METHOD

The interauricular septum of hearts with open, valvelike foramina ovale, removed at autopsy, is clamped by means of four screws between two flanged metal plates that have a circular opening completely exposing both sides of the foramen ovale. (Fig. 1.) Two glass cups (C) with three side openings are cemented to the flanges and function as artificial atria. Instead of blood, a fluid is used which consists of 0.32 per cent tragacanth suspended in 0.9 per cent saline. The viscosity and the osmotic pressure of this suspension are approximately that of blood. The height of the reservoirs (R) holding this fluid determines the auricular pressure which is measured by a straight manometer tube (M) connected with the artificial atrium by means of the middle side tube. The second side tube connects with the reservoir. The third side tube is clamped off and serves as a vent for the escape of air caught in the apparatus. Artificial emboli are prepared by mixing "Yatex"† (a concentrated form of Latex) with plaster of Paris in a proportion so that the small pieces ($1 \times 1 \times 2$ mm. to $2 \times 2 \times 3$ mm.) just about sink in the fluid. The mixture consists of 3.2 gm. Yatex and 1 gm. plaster of Paris. These pieces, ten to twenty in number, are introduced into the right atrium. Before each experiment the apparatus is tested for leakage, under a pressure of 400 mm. of fluid.

During the course of the experiment the height of the right reservoir is increased on several occasions so that various degrees of predominance in right auricular pressure are obtained. Due to the higher level of fluid in the right reservoir, a flow of the fluid is established through the foramen ovale from the right into the left reservoir. The heights of the fluid level in the reservoirs are recorded at the start and after one minute of flow. The auricular pressures as shown by the manometer in millimeters of fluid are also recorded at the start of the

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flow and during the flow. The change in volume in either reservoir during this time indicates the flow in one minute through the foramen ovale. Similar observations are made when the level of the left reservoir is raised higher than that of the right so that there is a predominance of pressure in the left atrium. During a period of flow under a maximum predominance of right auricular pressure the apparatus is shaken with both hands to agitate the artificial emboli in the right auricle. At the end of one minute of such flow, the emboli in the left auricle as well as the emboli caught in the foramen are counted.

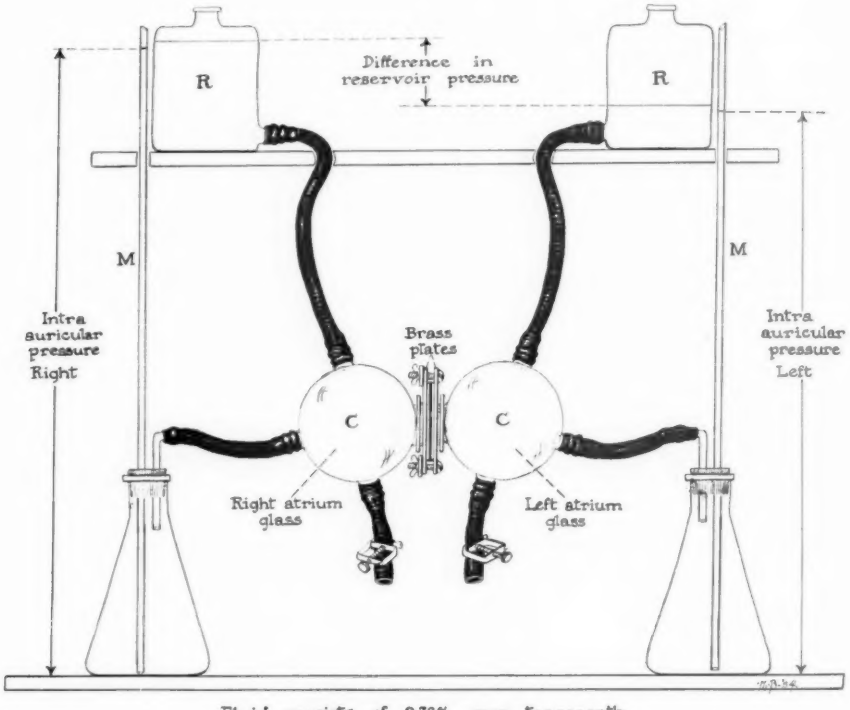

Fig. 1.—Diagram of apparatus.

RESULTS

With the fluid level of the right reservoir higher than that of the left reservoir and the tubing connecting with the left reservoir pinched off, the left auricular pressure may be equal to the right auricular pressure or may even exceed it. This paradoxical condition is explained by the fact that the foramen ovale behaves as a valve and transmits pressure freely in one direction only. As soon as the tubing to the left reservoir is opened, a drop in both auricular pressures occurs. This drop is greater on the left side. As the flow is maintained, the left auricular pressure begins to rise slowly while the right auricular pressure falls slowly. However, during the minute of flow, the right auricular pres-

sure is always greater than that of the left. When, at the end of one minute, the tubing to the left reservoir is again pinched off, both auricular pressures rise to a level commensurate with the fluid level in the right reservoir; and again the left auricular pressure may rise to a slightly higher level than the right because of the valvelike action in the foramen ovale. The fluid level of the right reservoir descends, while that of the left reservoir rises correspondingly from the time that the tubing to the left reservoir is opened to the moment that it is pinched

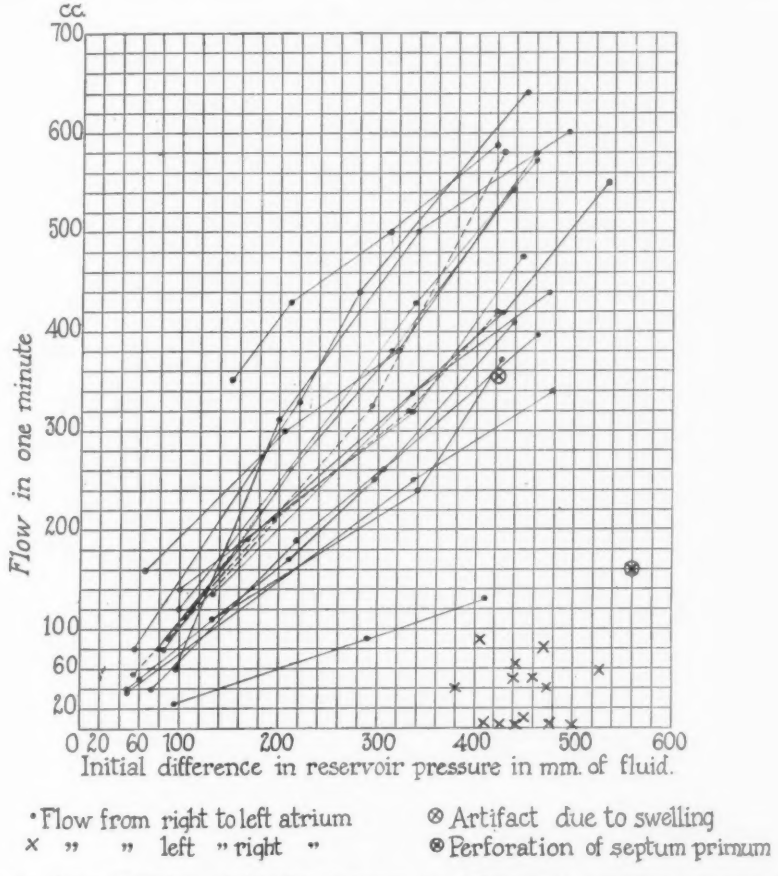

Fig. 2.—Graph showing relationship between the difference in reservoir pressure and the flow through the foramen ovale.

off again. The volume of flow from right to left increases with the degree of preponderance of right auricular pressure. The results of experiments performed on sixteen patent foramina ovale are listed in Table I. The graphical representation of the relationship between the leakage through the foramen ovale and the difference in reservoir pressure is shown in Fig. 2. It is seen that an almost linear relationship is indicated.

TABLE I

NO.	CIRCUMFERENCE OF FORAMEN	INITIAL PREDOMINANCE IN RIGHT RESERVOIR PRESSURE	TERMINAL PREDOMINANCE IN RIGHT RESERVOIR PRESSURE	INITIAL AURICULAR PRESSURES		AURICULAR PRESSURES DURING FLOW		TERMINAL AURICULAR PRESSURES		FLOW IN ONE MINUTE
				RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT	
	mm.	mm.	mm.							c.c.
1	30	425	265							590
		310	185							500
		210	105							430
		155	70							350
2	32	493	292	580	605	435	395	193	193	600
		339	205	619	619	500	465	357	357	500
		202	121	361	361	285	273	340	340	310
		97	9	51	51					64
3	Three small openings 1-2 mm. in diameter	426	318	592	592	440	360	383	383	420
		534	381	635	634	455	340	402	402	550
		195	143	366	366	290	263	270	270	210
		79	59	600	600	570	557	569	569	80
4	25	436	300	583	584	363	325	339	339	545
		316	229	581	582	424	395	414	412	380
		211	148	358	358	243	233	258	258	260
		81	60	587	585	544	535	540	540	80
5	40	452	290			390	375	227	227	640
		281	165			425	415	318	318	440
		221	137			283	268	192	192	330
		55	33			550	530	510	511	80
6	25	463	312	600	605	440	367	531	530	570
		337	228	600	602	485	430	547	548	430
		99	71	595	600	565	548	575	586	120
7	16	446	326			461	319			475
		336	248			460	387			320
		99	75			530	507			70
8	24	462	362	600	600	842	273	553	553	395
		305	235	545	545	455	352	490	490	250
		219	166	354	354	266	216	330	330	192
		74	40	515	515	532	517	552	552	40

TABLE I—CONT'D

NO.	CIRCUMFERENCE OF FORAMEN	INITIAL PREDOMINANCE IN RIGHT RESERVOIR PRESSURE	TERMINAL PREDOMINANCE IN RIGHT RESERVOIR PRESSURE	INITIAL AURICULAR PRESSURES		AURICULAR PRESSURES DURING FLOW		TERMINAL AURICULAR PRESSURES		FLOW IN ONE MINUTE
				RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT	
	mm.	mm.	mm.							c.c.
9	22	413	304	589	589	448	376	542	542	420
		332	245	588	590	474	417	548	548	320
		168	128	360	360	300	272	340	340	190
		87	67	586	590	555	546	578	582	90
10	28	439	352	558	558	385	352	514	514	410
		294	235	556	556	438	418	524	524	250
		210	157	327	327	240	228	304	304	170
		60	48	560	560	540	530	556	556	50
11	40	460	228	528	528	432	365	507	507	580
		320	238	278	278	454	426	244	244	380
		205	127	482	482	525	487	425	425	300
		65	40	568	568	555	545	508	508	160
12	12	425	332	145	145	450	124	187	187	370
		340	278	226	226	482	274	252	252	240
		133	92	496	494	578	507			105
		47	42	450	446	557	498	525	510	40
13	8	410	366	572	563	554	212	556	548	130
		290	273	558	552	492	274	523	510	90
		96	87	580	568	576	512	586	568	25
14	28	429	347	656	648	366	313			590
		293	196	560	670	416	388			325
		54	40	559	568	535	533			55
15	23	479	386	606	577	454	247			340
		337	271	608	577	497	338			250
		43	34	543	530	535	490			39
16	23	474	360	605	604	400	285			440
		338	248	590	606	453	378			335
		131	92	606	625	551	543			135

Occasionally emboli pass spontaneously through the foramen ovale, but generally emboli pass through the foramen ovale or are caught in it only after the apparatus has been shaken vigorously and the emboli thereby set into motion. Table II shows the relationship between the circumference of the foramen, the preponderance of the right auricular pressure, the preponderance of the right reservoir pressure, and the number of emboli which passed through, or were caught in the foramen ovale. No determination of the transmission of emboli was made on heart numbers 1 and 3. The only foramen ovale of those investigated which did not allow emboli to pass into or through it was number 13. The probable explanation for the behavior of this foramen is to be found in its small size.

TABLE II

NO.	CIRCUMFERENCE OF FORAMEN	PREDOMINANCE OF RIGHT RESERVOIR PRESSURE	PREDOMINANCE OF RIGHT AURICULAR PRESSURE	NUMBER OF EMBOLI CAUGHT IN FORAMEN	NUMBER OF EMBOLI WHICH PASSED THROUGH THE FORAMEN
2	32	680	230	0	9
4	25	437	–	0	2
5	40	281	10	0	1
5	40	221	15	0	2
5	40	452	15	0	3
6	25	456	103	1	0
7	16	447	–	5	0
8	24	474	–	3	2
9	22	332	60	0	1
9	22	413	72	1	2
10	28	439	33	3	2
11	40	460	67	2	3
12	12	425	326	1	0
13	8	410	342	0	0
14	28	429	53	0	5
15	23	479	159	0	4
16	23	510	–	7	4

When the predominance of pressure is shifted to the left side and the tube communicating with the right reservoir is pinched off, the right auricular pressure may correspond to the right reservoir pressure, or it may be higher. When the tubing to the right reservoir is opened, the right auricular pressure drops according to the fluid level of the right reservoir. In a few foramina ovale no subsequent increase in right auricular pressure occurs; nor is there a change in fluid level in either reservoir. In other words, some patent foramina ovale allow no leakage of pressure or fluid from left to right. In the larger number of cases, on releasing the pinched-off tubing, there is an immediate rapid drop of right auricular pressure to a level commensurate with the right reservoir fluid level. This is followed by a slight gradual rise in right auricular pressure accompanied by a slight drop in the fluid level of the left

reservoir and a coincidental rise in fluid level of the right reservoir. The greater the predominance of left auricular pressure, the greater the amount of leakage through the foramen ovale. With the exception of two instances, the amount of flow through the foramen ovale from left to right is slight compared with the flow from right to left at similar differences in pressure. The two discrepancies where considerable leak-

TABLE III

NO.	CIRCUMFERENCE OF FORAMEN	PREDOMINANCE OF LEFT RESERVOIR PRESSURE	AURICULAR PRESSURE DURING FLOW		FLOW IN ONE MINUTE
			RIGHT	LEFT	
1	30	445	No change		0
2	32	500	No change		0
3	Three small openings 1-2 mm.	474	115	569	40
4	25	423	290	468	355
5	40	561	83	550	162
6	25	470	156	582	83
7	16	529	173	571	58
8	24	450	46	592	10
9	22	406	278	486	90
10	28	380	—	—	40
11	40	460	—	—	50
12	12	425	No change		0
13	8	410	No change		0
14	28	442	163	506	66
15	23	476	133	603	0
16	23	440	155	555	50

age occurred from left to right are explained in one by a perforation in the septum, and in the other by a severe distortion of the foramen from edema secondary to clamping. The results of these investigations are tabulated in Table III and indicated in Fig. 2.

COMMENT

The results obtained indicate that the so-called anatomically patent, functionally closed foramen ovale transmits pressure, fluid, and suspended solids from the right to the left atrium when the right auricular pressure exceeds that of the left. These findings are in accord with the observations and conclusions of Zahn,[1] Mönckeberg,[2] Beattie,[3] French,[4] Chiari,[5] and others.

Zahn collected 139 cases which at autopsy had a patent foramen ovale. Among these cases, he found two with thrombotic occlusion of the foramen and seven with paradoxical embolism. In addition, he listed a third case, referred to him, of thrombotic occlusion of the foramen ovale. Zahn believed the explanation of paradoxical embolism to lie in the fact

that in congestive heart failure there is an elevation in right auricular pressure with a coincidental reduction in left auricular pressure. In all nine cases, evidence of venous stasis conditioned by chronic bronchitis, pulmonary emphysema, edema, atelectasis, tuberculosis or pleuritis was found. The anatomical evidence pointing to a previously existing congestion and elevation of pressure in the right heart consisted of dilatation and hypertrophy of the right auricle and ventricle, the enlargement of the fossa ovalis and the bulging of its wall to the left.

Beattie reported a case of pulmonary embolism which, at autopsy, showed occlusion of the pulmonary artery by an embolus and a second embolus caught in the foramen ovale. This foramen ovale was of the type considered anatomically open but functionally closed. Beattie inferred that the embolic occlusion of the pulmonary artery preceded the embolic occlusion of the foramen ovale. He contended that the embolic occlusion of the pulmonary artery caused an elevation of the right auricular pressure and a coincidental fall in the left auricular pressure which forced the foramen ovale open and allowed the second embolus to slip in and lodge there. He indicated that in all probability the reason for the patient's survival for a short time after the pulmonary occlusion was the patent foramen ovale which allowed the blood to be shunted across to the left atrium. He suggested that patency of the foramen ovale be kept in mind to explain similar short survivals following pulmonary occlusion.

The apparatus used in these investigations does not reproduce the rapid movement of fluid with eddies which are present in the living heart. It is therefore necessary to agitate by shaking, but this also appears inadequate. It is possible that with a modification of the apparatus to provide for a brisk flow of the fluid with a production of eddies, a larger number of emboli would pass through the foramen ovale under the same pressure conditions.

A valvelike action of the foramen ovale is established by its capacity, in some cases, to prevent completely the leakage of pressure and fluid from left to right, and in other instances to transmit comparatively very little fluid to the right atrium. This valvelike action is due to the tenuity and pliancy of the septum primum and the relative thickness and rigidity of the septum secundum.

There are no data available on human left and right auricular pressures, and the pressures used in these experiments may very well be beyond the pathological limits occurring in man. Nevertheless, the behavior of this type of foramen ovale under these experimental conditions is probably a good indication of the behavior clinically under certain pathological conditions.

CONCLUSIONS

These investigations on the so-called anatomically open but functionally closed foramen ovale furnish experimental proof for the following statements:

1. Under conditions of preponderance of pressure in the right atrium over the left, pressure, fluid, and emboli may be transmitted from the right atrium through the foramen ovale into the left atrium.

2. When the left auricular pressure is greater than the right, comparatively little or no transmission of pressure or fluid from the left atrium to the right atrium occurs due to a valvelike action of the foramen ovale.

The author thanks Dr. H. S. Reichle and Dr. Morris Simon for aid in securing material.

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THE ELECTROCARDIOGRAM OF THE NORMAL HEART IN PREGNANCY*

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IF THE electrocardiogram is to aid us in the interpretation of the signs and symptoms referable to the cardiovascular system in pregnant women, we must be acquainted with the influence that pregnancy, due to a rising uterus, may have on it.

That the electrocardiogram undergoes certain changes when the position of the heart within the chest is altered, has been long appreciated. Einthoven showed that deep breathing affected the form of the electrocardiogram, as it changed the position of the heart, the more transverse position at the end of expiration being associated with a left axis shift, or a tendency in that direction. Cohn demonstrated that there is a rather definite relation between the anatomical angle of the heart (angle of inclination) and the direction of the electrical axis. Thus the electrocardiogram shows a gradually increasing left axis deviation as the position of the heart becomes more transverse, and right axis deviation as the heart becomes more vertical.

But that pregnancy may change the electrical axis of the heart by a rising diaphragm is not widely known. Smith showed that during the eighth month of pregnancy when the uterus is at the highest level in the abdomen, the electrocardiogram displayed a left axis deviation. This became less marked as soon as the head of the fetus descended into the pelvis, and shifted toward the right immediately after the delivery of the child. Konki studied 33 pregnant women with normal hearts, and he found that during the third trimester of pregnancy, the electrical axis deviated to the left, and that the T-wave in Lead III became negative. Following the delivery the axis shifted to the right, and the T-wave in Lead III became upright. He quotes Hynemann, who affirms that the diaphragm of pregnant women during the early part of the third trimester is elevated on the right side on the average of 2.10 cm. and on the left side by 2 cm. and that the heart has assumed a more transverse position. Jensen and Norgaard reported that in their series of pregnant women there was a left axis deviation or a tendency thereto during the first months of pregnancy and a return to the right in the later months. They say that this is due to an early left ventricular hypertrophy, followed later by a right ventricular hy-

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pertrophy, independent of any change in the position of the heart. These observations led us to study the electrocardiogram in pregnancy.

After we began our investigation, an article appeared by Carr and Palmer, who found that the axis tends to shift to the left during the first two trimesters of pregnancy and to the right in the early part of the ninth month. The latter finding they attribute to the descent of the uterus.

Material.—Thirty-six pregnant women were selected. These patients had no complaints referable to their cardiovascular system, and upon examination their hearts and vascular systems were found to be normal. In selecting these patients, age and the number of the pregnancy were not considered. These women were sent down to the electrocardiographic laboratory some time between the thirty-second and thirty-sixth weeks of pregnancy, when the uterus was considered to be at the highest level in the abdomen. This procedure was strictly supervised by one of us (H.H.H.). The second electrocardiogram was taken about eight or ten days after delivery when the patient was ready to go home. At first we took a third electrocardiogram, six weeks post partum. But the latter was soon abandoned, since we found no difference between it and the second electrocardiogram. The electrocardiograms were taken with the patient in the sitting position. The electrical axis was calculated, according to Einthoven, from the electrocardiogram.

RESULTS

Direction of the Electrical Axis.—The influence of pregnancy on direction of this axis is shown in Table I. Only those tracings showing a shift of more than 10 degrees in the electrical angle were recorded. Twenty-one of the 36 cases studied (58.33 per cent) showed such changes.

It will be seen that there is usually definite shifting of the electrical axis toward the left during this period of pregnancy, and to the right in the puerperium. The first case has an angle of –2 degrees which is slight axis deviation (considering 0-90 as normal). Following the delivery the angle changed to 49, which is normal. The next two cases with an electrical axis of "0" may be considered as having a tendency to left axis deviation. Their axis, too, became normal following the delivery. Cases 4, 5, 6 and 7 may be considered as having only a slight tendency toward left axis deviation, which became normal after the delivery. The next six cases are, as considered by some,[7] at the lower limits of normal. The greatest shifting of the axis toward the left was noticed in Case 9. Before delivery the angle was 10 degrees and after delivery 90 degrees; in other words from the lower to the very upper limits of normal. Cases 14, 15, 16 and 17 had each an angle of 30 degrees before delivery. During the first week of puerperium this angle changed to 72°, 58°, 55°, and 60° respectively. Cases 18, 19, 20

and 21 had angles which are considered just normal, and the shift to the right following delivery was not very marked, the largest being 20° and the smallest 13°. Thus, in the entire series the shift to the right in puerperium varied from one of 13° to one of 80°. The average direction of the electrical axis between the thirty-second and thirty-sixth weeks of pregnancy in this series was 19°, and a week after the delivery 57°. The average difference, thus, in the axis was 38° in a counter-clockwise direction, or shifting to the left. This figure is greater than that reported by Carr and Palmer, whose difference is only 27° to the left in four cases in which an electrocardiogram was taken after delivery.

TABLE I

INFLUENCE OF PREGNANCY ON DIRECTION OF THE ELECTRICAL AXIS AND ON T_3-WAVE IN THE NORMAL HEART

	PREGNANCY 32-36TH WEEK		PUERPERIUM FIRST WEEK		DIFFERENCE IN THE ANGLE
CASES	ANGLE	T_3*	ANGLE	T_3*	ANGLE
1	−2°	−	49°	−	51°
2	0	±	58°	+	58°
3	0	−	43°	±	43°
4	3°	−	52°	+	49°
5	3°	−	52°	−	49°
6	3°	−	52°	−	49°
7	4°	−	30°	−	26°
8	10°	−	50°	+	40°
9	10°	−	90°	±	80°
10	12°	−	52°	±	42°
11	15°	−	55°	−	40°
12	17°	−	50°	−	33°
13	18°	+	65°	+	48°
14	30°	−	72°	−	42°
15	30°	−	58°	−	28°
16	30°	−	55°	−	25°
17	30°	−	60°	−	30°
18	40°	0	58°	+	18°
19	42°	−	62°	−	20°
20	51°	−	64°	+	13°
21	53°	+	70°	+	17°
Averages	19°		57°		38°

*+means upright.
− means inverted.
± means diphasic.
0 means flat or isoelectric.

Our results correspond with those of the authors mentioned, although our procedure was somewhat different. Taking into consideration what is known about the influence of the position of the heart on the electrocardiogram, it is logical that, at a certain stage of pregnancy, when the diaphragm is very often pushed up so that the heart lies in a comparatively transverse position, there should be a shift of the electrical axis to the left. (Fig. 1.) The type of the individual also plays a great part; the hypersthenic patient during pregnancy will show more deviation to the left than will the opposite type. This factor, besides the size of the baby and the amount of amniotic fluid, may be responsible for the

difference in the degree of the shift in different patients, or for the absence of an appreciable deviation in others. That is, a fairly high diaphragm with a small uterus may produce more shifting than a low diaphragm with a good-sized baby.

Recent studies in obesity[8, 9] show that the position of the diaphragm is often responsible for left axis deviation and changes in Lead III. The electrocardiogram returned to normal in the great majority of patients

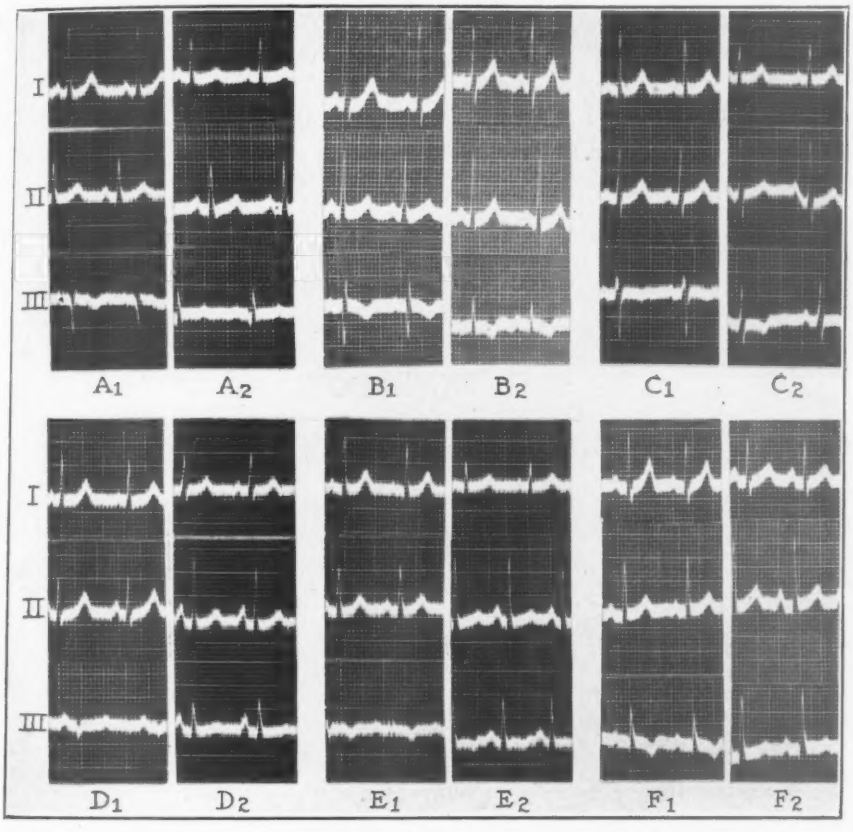

Fig. 1.—Six pairs of electrocardiograms to show the variations which may be encountered in Lead III during pregnancy. In each case, the first electrocardiogram was taken between the thirty-second and thirty-sixth weeks of pregnancy and the second during the first week of the puerperium.

who lost weight by dieting. Kimura studied the roentgenograms and the electrocardiograms of patients with big ovarian tumors. The heart occupied a more or less transverse position in the chest, and the electrocardiogram showed a tendency to left axis deviation. The T-wave in Lead III became flattened or inverted. After removal of the tumor the heart became more vertical, and the electrocardiogram shifted toward the right, and the T-wave in Lead III assumed an upright position

Bland and White in studying one hundred electrocardiograms with complete inversion of Lead III showed that 72 per cent of the patients had a high diaphragm and a transverse position of the heart, and that 55 of these were obese individuals. All these studies tend to show that it is the position of the heart and not the questionable transient hypertrophy that is responsible for the shifting of the axis toward the left.

Changes in the P-wave in Lead III.—We have encountered two records with an inverted P_3. One was associated with an inversion of the entire Lead III, besides an inverted P_2, and the other occurred in an otherwise normal electrocardiogram. Both remained unchanged during the puerperium, in spite of the fact that the other complexes of the inverted lead, as well as the inverted P_2, became upright. There was a definite tendency, however, for the P-wave in Lead III to become more defined and of a somewhat higher voltage after the delivery. However, it seems that the influence of pregnancy on the P-waves is only slight and of little significance.

Changes in the Q-wave in Lead III.—Five records with large Q-waves in Lead III, according to the criteria of Pardee, were found in this series of 36 cases. They were all associated with inverted T_3. Three of these large Q-waves in Lead III disappeared after pregnancy (see B_1 and B_2, Fig. 1). In one of these the negative T-wave in Lead III became flattened, and the R_3 became somewhat higher. In the remainder the T_3 was not changed. According to the recent literature,[13, 14] the large Q-wave in Lead III during pregnancy is taken to signify a transverse position of the heart due to elevation of the diaphragm. That the deviation of the septum from its usual position, as well as the transverse position of the heart, may be a factor in the production of Q_3, has been suggested.[14] The incidence of the large Q_3 in our series is about the same as that reported by others. It is of interest that the incidence of the larger Q_3 in normal hearts in pregnancy is very much greater than in normal hearts in a control series.[12, 13] Evidently the altered position of the heart is a large factor in this change.

Changes in T-wave in Lead III.—Of the 21 cases that showed marked changes in direction of the electrical axis, T_3 was completely inverted in 17; in one it was flat, in one diphasic and in two upright. During the puerperium the T_3 was negative in 11 cases, diphasic in 2, and upright in 8; in other words a gain of one diphasic T_3 and 6 upright ones. (See Table I.) Left axis deviation or tendency thereto, due to a change in position of the heart, is usually associated with an inverted T_3.[2, 11] Our records bring this out. Table I shows that the first upright T in Lead III is seen in Case 13, whose angle is 18°. The next one is seen in the last case, whose angle is 53°. During the puerperium the appearance of the upright T-wave in Lead III was usually associated with angles

of 50° or over, which is considered normal. On the other hand, in no instance did a positive T_3 during pregnancy become changed after the delivery.

There were four records which showed no changes in the electrical axis but had negative T_3. After the delivery, one such became diphasic, one flat and two upright. Hence by adding these two groups showing changes in T_3 we find that out of 25 records, an inverted T_3 was seen in 21 patients before delivery and only in 11 after—a change of 47.61 per cent toward the upright.

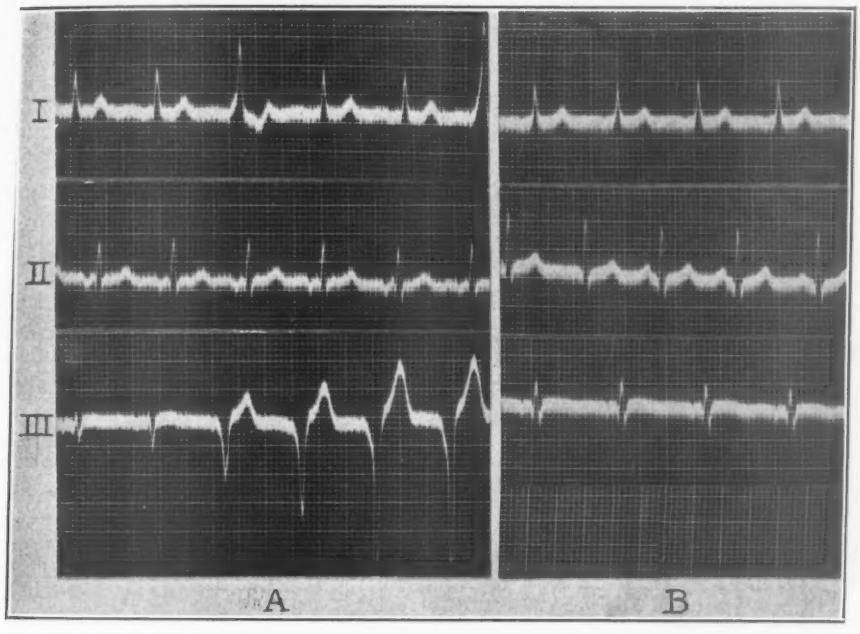

Fig. 2.—*A*, Two electrocardiograms of the same patient. *A* was taken between the thirty-second and thirty-sixth weeks of pregnancy. Rate is 105. Frequent extrasystoles in Lead I, and P_2 and P_3 are inverted. Lead III shows a run of ventricular tachycardia.

B was taken during the first week of puerperium. Rate is 96. Arrhythmia disappeared. P_2 has become positive. Note the change of the direction of the electrical axis.

Pardee states that a downward T_3 may be due at times to a high position of the diaphragm. This would tip the apex of the heart upward and would tend to produce a relatively small or even inverted T_3, just as it tends to produce a small or inverted R_3. The variations in the direction of the electrical axis within the heart, giving rise to the T-wave are modified by the position of the heart in the body. The changes in the T-waves in Lead III in our series can probably be accounted for by the high position of the diaphragm. Thus the heart has moved, as we view the patient from the front, in a counter-clockwise direction when

the uterus has reached its highest level in the abdomen, and in a clockwise direction as soon as the uterus has emptied itself.

Arrhythmia.—One of our records showed frequent ventricular extrasystoles terminating in a short paroxysm of ventricular tachycardia. This was observed on several occasions between the thirty-second and thirty-sixth weeks of pregnancy. The rate per minute was over 100 each time, and the patient was very uncomfortable. She was conscious of these "skipped beats," and she experienced some dyspnea. In the electrocardiogram taken after the delivery, the arrhythmia was absent, and the pulse rate was lowered somewhat (Fig. 2). The symptoms also disappeared. Premature contractions have been known to exist during pregnancy and labor. According to Mackenzie, this arrhythmia occurs very frequently during pregnancy. It is of interest to note that the comparatively rapid heart in our patient did not prevent the appearance of these premature contractions. It is possible that some product of the metabolism in pregnancy is responsible for the production of this arrhythmia.

SUMMARY

1. The electrocardiograms of 36 pregnant women with normal hearts were studied. One electrocardiogram was taken some time between the thirty-second and thirty-sixth weeks of pregnancy, and a second during the first week of puerperium.

2. Twenty-one cases (58.33 per cent) showed a left axis deviation or tendency thereto during the time when the uterus was at its highest level in the abdomen. The smallest deviation in a counter-clockwise direction was 13° and the largest was 80°, the average being 38°. The axis shifted to the right following delivery.

3. An inverted T_3 was seen in 17 of the 21 records showing axis deviation. Two were positive, one was isoelectric, and one was diphasic. During the puerperium there appeared only 11 inverted, 8 positive, and 2 diphasic T_3. Four records, not showing any change in the axis, showed T_3 inverted during pregnancy, and after delivery in two instances this became upright, in one isoelectric and in one diphasic (11.11 per cent).

4. Three records of the 36 (8.33 per cent) showed a large Q_3 which disappeared following the delivery.

5. One case (2.61 per cent) had frequent ventricular extrasystoles, terminating in a short run of ventricular tachycardia. After the delivery this arrhythmia disappeared.

6. Adding the changes seen in the axis, T-waves alone, the large Q_3, and one case of arrhythmia, we have an incidence of 80.88 per cent in our series that showed changes in the electrocardiogram during a time when the uterus was at its highest level in the abdomen. (Table II.)

7. These findings corroborate those found in the literature and are compatible with the interpretation that during this stage of pregnancy

the heart assumes a comparatively transverse position due to the elevation of the diaphragm.

TABLE II

THE INCIDENCE OF CHANGES IN THE ELECTROCARDIOGRAM OF THE NORMAL HEART IN THIRTY-SIX PREGNANT WOMEN

CHANGES	CASES	PER CENT
Changes in angle and T_3	21	58.83
Large Q in Lead III	3	8.33
Changes in T_3 alone	4	11.11
Changes in rhythm	1	2.61
Total	29	80.88%

8. When interpreting an electrocardiogram of a pregnant woman, one should bear in mind that at a certain stage of pregnancy left axis deviation, or tendency thereto, may often be found; that a large Q_3 may frequently be seen; and that extrasystoles are not rare. These findings disappear as soon as the uterus empties itself.

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Department of Clinical Reports

ELECTROCARDIOGRAMS FROM A FOUR AND A HALF MONTHS OLD FETUS

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THE diagnosis of incarcerated retroversion of a four months' pregnant uterus with threatened abortion was made on a twenty-seven-year-old colored woman, and laparotomy was decided upon. Dr. Martha Elizabeth Howe and I made preparations to take electrocardiographic tracings of the fetus, hoping at first that this could be done with the fetus in the uterus, before the removal of the uterus from the abdomen. However, at operation the findings were as follows:

The rectosigmoid junction and a fresh left pus tube were densely adherent to the anterior surface of the uterus, 1 cm. above the vesical fold of the peritoneum. In separating the adhesions the uterine wall had to be sacrificed to save the intestine, and a ragged tear was thus made with free bleeding and protrusion of the placenta. A supravaginal hysterectomy and bilateral salpingectomy were performed without, of course, opening the uterus in the abdomen.*

Immediately after removal, the uterus was opened, and the fetus, measuring 21 cm. in length, was removed, the connection between fetus and placenta being allowed to remain intact. The heart could be seen to be beating vigorously and continued to contract for approximately forty-five minutes. During this period we obtained the accompanying tracings.

Ordinary copper wire was used for electrodes, one end of the wire being inserted under the skin and the other end attached to the lead cables of a Sanborn portable electrocardiograph. The first three electrocardiograms were obtained with one electrode at the apex of the heart and the other just below the angle of the left scapula. An effort was made to obtain limb leads also, but only Lead II could be successfully recorded.

Tracing *A* was taken with the fetus attached to the placenta; that is, with the umbilical cord intact. *B* was taken with the cord firmly clamped. The general contour of the complexes is very similar to those

*The gynecological data were supplied by the operator, Dr. F. S. Fetterman.

of *A*, but the T-wave is less deeply inverted. *C* was taken several minutes later when the rate was beginning to slow. *D* was taken with the electrodes inserted under the skin of the right wrist and left ankle.

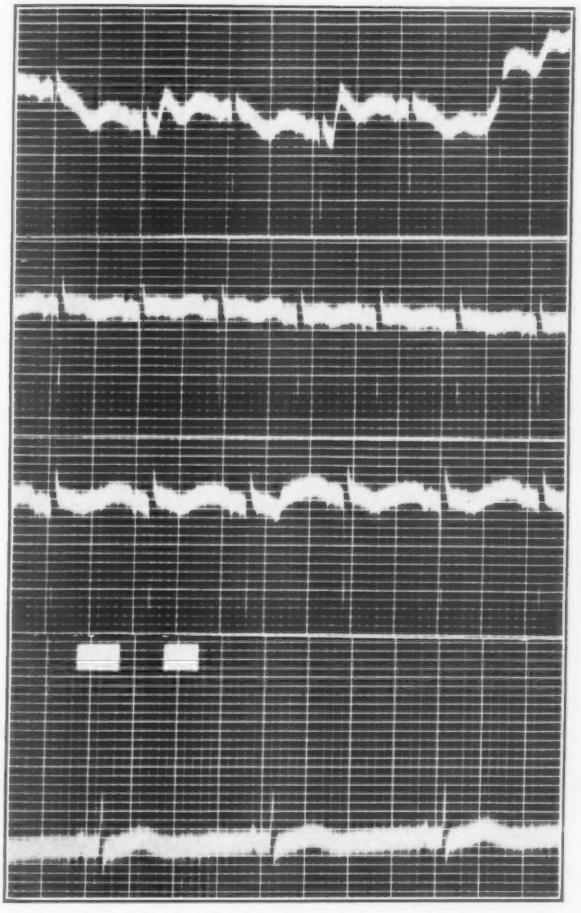

Fig. 1.—Electrocardiograms from a four and one-half months' fetus. *A*, *B* and *C*. chest leads—*A*, fetus attached to placenta; *B*, umbilical cord clamped; *C*, same as *B*, several minutes later, rate slowing. *D*, limb lead (right arm, left leg).

In general contour and direction of complexes it resembles the adult type of electrocardiogram.

As far as I have been able to ascertain, no electrocardiographic records from so young a fetus have been published prior to this time.

FREE BALL THROMBUS OF THE LEFT AURICLE*

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THE presence of a free ball thrombus in the heart is so rare as to be classed almost as a clinical and pathological curiosity. According to Covey, Crook, and Rogers,[1] twenty-three cases had been reported up to the appearance of their paper in 1928. These, together with their case, plus those of Schwartz and Biloon[2] and ours, make a total of twenty-seven, of which thirteen were diagnosed or suspected during life. According to the criteria of Hewitt,[3] the two chief requirements for this diagnosis are that (1) it must be larger than the orifice in front of it, and (2) it must have a smooth surface and show no signs of former attachment. A number of thrombi have been wrongly considered as free when in reality they have been accidentally torn loose from their attachment by the manipulations of the pathologist in opening the heart. Practically, it is a matter merely of academic interest to distinguish, if it were possible, between a free thrombus and a pedunculated one, since both can act in the same way in producing symptoms.

It is our purpose to present an additional case and to discuss a few of the salient points in the clinical picture and the diagnosis.

REPORT OF CASE

A. K., female, fifty-three years old, was admitted to the Jewish Hospital on March 26, 1932, complaining of generalized aches, pains, and fever. Four days previously she had had dizzy spells and had become white and cold. There had been nausea and vomiting as well as some fever and cough for two days. She dated her first symptoms eight years before this entry when she began to have precordial pain and palpitation. Five years after the onset of her first symptoms she had been admitted to the hospital with the heart severely decompensated. At that time the diagnosis of auricular fibrillation, chronic myocarditis, and chronic passive congestion of the liver and lungs was made. With rest in bed and digitalization she quickly improved and was discharged from the hospital.

On her present admission she was deeply cyanotic and dyspneic, the heart was enlarged, and a systolic murmur was heard over the whole precordium, rougher over the aortic area than elsewhere and transmitted to the neck vessels. Mitral stenosis as indicated by a presystolic apical murmur and auricular fibrillation were present, the apex and radial rates being 84 per minute. Over the lungs, which were emphysematous, coarse rhonchi were heard which later disappeared. The abdomen was tympanitic, and the liver was felt two fingerbreadths below the costal margin. The reflexes were normal, no pathological toe signs being elicited. She was given relatively small doses of tincture of digitalis (1 c.c. daily) and became comfortable and symptom-free for the next ten days when she was allowed to be up and about.

*From the medical service of Dr. L. Sale, Jewish Hospital of St. Louis.

On April 7, 1932, she began to complain of sudden pain in both lower extremities and of marked coldness of the legs and cried out that she was dying. The arms and hands were found to be cold, while the finger tips were slightly cyanotic. In addition, too, the legs were cold, pale, cyanotic, and there was tenderness over the tibial ridge. The dorsalis pedis, popliteal, and femoral pulsations could not be felt. The pupils were dilated and reacted to light and accommodation. The heart was generally enlarged; the apex and radial rates were 72. On auscultation the precordial murmur was unchanged, and the second sound was accentuated everywhere. The blood pressure was 230/80 mm. It was thought that she had developed an embolus just above the bifurcation of the aorta. The next day both lower extremities were cold and pale from just below Poupart's ligament downward, the right leg being a trifle mottled. There was well-marked hyperesthesia from the middle of the thighs to the knees, while from the knees downward there was anesthesia. The femoral, popliteal, and posterior tibial pulsations remained impalpable. On the third day there was no indication of gangrene, the color of the legs had improved, and except for the toes the extremities had become warm, an improvement which had become definite within forty hours of the onset of symptoms.

On April 17, 1932, she suddenly began to gasp for breath and complain of chest pain. She was found sitting up, breathing hurriedly and heavily, apparently in agony. The chest pain was localized to the lower precordium. Her complexion was as usual, and examination of the heart revealed no new findings. The right radial pulse was markedly weaker than the left; the blood pressure could not be obtained on the right arm, while on the left it was 220/90. This attack quickly subsided, and it was at this time that the presence of an occluding ball thrombus of the left auricle was suspected for reasons which will be discussed later. The next day the right radial and brachial pulsations were still very feeble, but the arm was warm and seemed to be somewhat spastic.

She steadily lost ground, getting weaker and the extremities becoming quite cold again. The pulse could hardly be palpated anywhere, and she lapsed into coma, dying April 25, 1932, eighteen days after the onset of symptoms of peripheral circulatory disturbance and thirty days after her admission.

Autopsy Findings.—The pertinent findings at the post-mortem examination which was done by Dr. Sam Gray were as follows:

Heart: The heart was somewhat enlarged, the hypertrophy occurring chiefly in the right ventricle. The musculature of the left auricle was also hypertrophied. The tricuspid, pulmonary and aortic valves were thin and delicate and presented no deviation from the normal. The mitral valve was very thick and hardened, and the leaflets were fused, presenting at its opening a mere slit measuring 4 × ½ cm. The chordae tendineae were short and thick.

Within the left auricle there was a moderately firm, slightly oval, smooth-surfaced thrombus measuring 7 × 5 cm. A thin, recently formed post-mortem blood clot adhered to one edge of the thrombus and extended on to the ear of the auricle. After a careful search no small thrombi or areas of endocardial roughening were found. Upon section the central part of the thrombus was beginning to undergo softening, although as yet it was still compact.

Aorta: In the aorta from above the origin of the celiac axis and extending down for 2 cm. into the right iliac and 4 cm. into the left iliac artery there was a thrombus completely occluding this vessel. Sections taken through the aorta and iliac arteries showed the oldest part of the thrombus to be that in the left iliac artery and the lowermost portion of the aorta. The remainder probably is a propagated thrombus.

The uppermost part of the thrombus is smooth. The axillary arteries were opened from their beginning to a distance about halfway down the arm, but no thrombus was encountered. A probe passed further down met no resistance.

Lungs: No significant changes were found.

Spleen: The spleen was firm and presented one small depression, probably the result of a healed infarct.

Kidneys: The left kidney presented several deep depressions, probably the result of previous infarcts. The right kidney had several rather fresh infarcts with the typical yellowish area of necrosis and a zone of hemorrhage about it.

Pathological diagnosis.: (1) Free ball thrombus of the left auricle, (2) thrombosis of abdominal aorta, (3) mitral stenosis, (4) infarcts of kidneys and spleen, (5) chronic passive congestion of viscera.

COMMENT

In 1896, Von Ziemssen[4] suggested for the first time, from a study of three patients, the possibility of diagnosing occluding auricular thrombi clinically. He stated that the criteria upon which the diagnosis could be made were: (1) absent or decreased pulsations in the peripheral vessels, (2) circumscribed gangrene of the feet, and (3) cadaveric coldness and swelling of the legs.

Since then, cases diagnosed clinically and confirmed by autopsy have been reported by Bozzolo[5] in 1896, Lutembacher[6] in 1917, Auberton and Rime[7] in 1926, Covey, Crook, and Rogers[1] in 1928, Schwartz and Biloon[2] in 1931, and the one which we are presenting.

From examination of the case reports and the experience with the one presented by us, we are in accord with the opinion expressed by Schwartz and Biloon and others that the clinical diagnosis of a ball or pedunculated thrombus of the left auricle can be made and is justifiable under certain conditions. No conclusions could be drawn from the history alone, although the presence of a long-standing mitral stenosis together with auricular fibrillation, which were present almost invariably in the reported cases, adds somewhat to the possibility of this diagnosis. With a very few exceptions the signs over the heart itself are not unusual and do not aid us in determining the presence of this condition. The most important diagnostic feature, in our opinion, is the presence of the comparatively rapid and transitory changes in the peripheral circulation, such as marked cyanosis or even gangrene which may involve the finger tips, toes, or tip of the nose. Cadaveric coldness may occur suddenly, and quickly improve or disappear. The disappearance or diminution of pulsations, not from one extremity but from several of them, including both upper and lower, and their relatively rapid restoration as occurred in our case should be emphasized. Such symptoms cannot be explained on the basis of peripheral emboli alone. Moreover, it is unusual for peripheral thrombotic emboli to be given off to such wide-spread areas simultaneously. They can, however, be explained

by the presence of a ball thrombus in the left auricle which temporarily obstructs the flow of blood into the ventricle with consequent serious wide-spread impairment of peripheral circulation. With dislodgment of the thrombus, the symptoms and signs improve or disappear, the pulsations in the extremities return, the color becomes better, and the legs and arms become warm. These peripheral phenomena may be caused in two ways: (1) by obstruction of the mitral orifice with the ball thrombus, or (2) by the presence of emboli in the peripheral circulation together with the auricular ball thrombus, as occurred in the case we have described.

CONCLUSIONS

A case of free ball thrombus of the left auricle suspected ante mortem is presented, and the possibilities of making a diagnosis clinically are discussed.

The diagnosis is frequently impossible, but it can sometimes be made on the basis of (a) long-standing mitral stenosis usually with auricular fibrillation, and (b) wide-spread and transitory disturbances in the peripheral circulation.

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UNUSUAL MANIFESTATIONS FOLLOWING THE USE OF QUINIDINE SULPHATE IN A PATIENT WITH AURICULAR FLUTTER*

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THE following case of transient amblyopia and of an ectopic rhythm resembling ventricular tachycardia, following the administration of quinidine sulphate during the presence of auricular flutter, is of unusual interest.

REPORT OF CASE

B. G., a Jewish female, aged forty-five years, was admitted to the Montefiore Hospital on April 10, 1933, with a history of recurrent episodes of palpitation of the heart. Her heart rate varied between 110 and 220 beats per minute, and electrocardiograms revealed the underlying cardiac mechanism to be auricular flutter with a variable ventricular response. Congestive heart failure, such as enlargement of the liver and edema of the lower extremities, appeared when her heart rate remained elevated. Digitalis, administered in large doses, did not abolish this rhythm.

On April 19, 1933, two test doses of 0.2 gram each of quinidine sulphate were administered at a four hour interval. Following the second dose the patient complained of severe headache, dizziness, and nausea. The drug was then discontinued. She continued to show auricular flutter (Fig. 1-1). Digitalis was again given in 0.2-0.3 gram daily doses, but there was no effect on the heart rhythm. The paroxysms of 1:1 flutter continued unabated, and the condition of the patient became desperate.

On May 9, 1933, a probatory dose of 0.2 gram of quinidine was again given, and this time there were no toxic manifestations. A 0.2 gram dose of quinidine sulphate was then given every two hours for 8 doses on this day, and this dosage was repeated on the following day. The rate of the auricles persisted at 220 beats per minute, and the ventricular rate remained at 110 beats per minute. The total amount of the drug given on May 9 and 10 was 3.2 grams.

On May 11, 1933 (third day), after 6 similar doses had been given over a period of twelve hours, there was an increase in the ventricular rate to 204 beats per minute. The drug was then given every hour in the 0.2 gram doses until the following afternoon. At 2 P.M. of the next day (May 12, 1933) the flutter waves in the neck veins were no longer visible. The heart rate was 75 beats per minute. An electrocardiogram confirmed the presence of sinus rhythm with a marked increase in the P-R interval to 0.32 second (Fig. 1-2). The total amount of the drug given on May 11 was 3.6 grams.

The sinus rhythm persisted until 7 P.M. when, after slight exertion, there was a sudden rise in the heart rate to 180 beats per minute. The flutter waves were again seen in the neck. The hourly administration of quinidine, which had been discontinued one hour with the onset of sinus rhythm, was again resumed. The

*From the Medical Division of the Montefiore Hospital, Service of Dr. Leopold Lichtwitz.

ventricular rate now fell to 100 beats per minute but the rhythm was irregular, the irregularity being due to a variable ventricular response in the presence of auricular flutter. The total amount of the drug given on May 12 was 3.2 grams.

On May 13, 1933 (fifth day), only 5 doses of 0.2 gram of quinidine were given at two hour intervals. The administration of the drug was then discontinued for the day because numerous premature beats were observed in the electrocardiogram. The total amount of the drug given on May 13 was 1.0 gram.

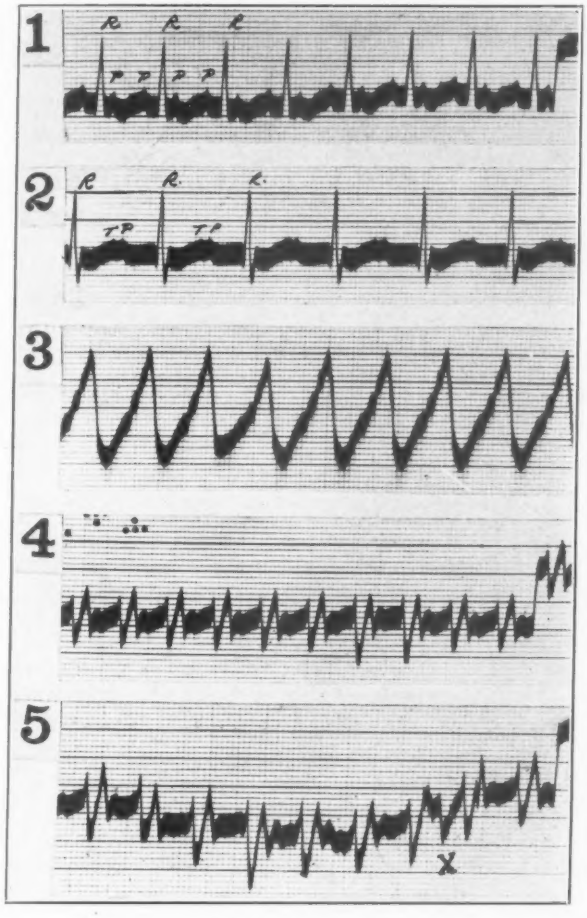

Fig. 1.—Lead I.

On May 14, 1933 (sixth day), the ventricular rhythm was again regular, the ventricles beating at 110 per minute and the auricles at 220. The patient received 0.2 gram of quinidine hourly for 4 doses, and then the interval between doses was increased to two hours. The total amount of the drug given on May 14 was 2.8 grams.

On May 15, 1933 (seventh day), the auricular flutter persisted, and the ventricular rate ranged from 80 to 110 beats per minute with a varying degree of block. During this day, however, multiple premature ventricular beats were again noted, and the

drug was temporarily discontinued after two doses of 0.2 gram each given at a two hour interval. The total amount of the drug given on May 15, was 0.4 gram.

On May 16, 1933 (eighth day), the ventricular rate ranged from 85 to 110 beats per minute, and the auricles still fluttered at a rate of 200 beats per minute until 2:30 P.M. when the ventricular rate suddenly increased to 220 beats per minute and the patient's pulse could not be felt. Quinidine sulphate was now again administered in 0.2 gram doses every hour. The ventricular rate fell to 100 beats per minute after two hours and remained at that level until late in the evening when there was another sudden rise to 200 beats per minute. Electrocardiograms at this time showed auricular flutter with a 1:1 ventricular response. The total amount of the drug given on May 16 was 1.8 grams.

On May 17, 1933 (ninth day), at 6 A.M. the degree of auriculoventricular nodal block increased, and the ventricular rate fell to 105 beats per minute. The patient was given hourly doses of 0.2 gram of quinidine sulphate. The ventricular rate remained at 100-110 until 8 P.M., when it again increased to 200 beats per minute. A 0.4 gram dose of quinidine sulphate was administered at hourly intervals for two doses, when the patient began vomiting; the drug was then discontinued. The total amount of the drug given on May 17 was 4.8 grams.

During that night the ventricular rate varied from 140 to 160 beats per minute and the patient went into circulatory collapse early the following morning.

On May 18, 1933 (tenth day), the respirations were Cheyne-Stokes in type; the lungs had filled up with moisture; and the ventricular rate persisted at 160 beats per minute and was regular. Metaphyllin solution, 2 c.c., was given intravenously with an immediate return to normal respirations. Early in the afternoon the patient regained consciousness. Later that afternoon she complained of inability to see. The fundi did not show any changes, and the neurological examination was also negative.

The electrocardiogram (Fig. 1-3) taken in the morning when the rate was 120 beats per minute showed an aberrant ventricular complex in the presence of a slow ventricular rate. However, the possibility of a ventricular response to every second auricular flutter impulse, with deformed ventricular complexes due to quinidine poisoning in the conduction mechanism in the ventricles must be considered, especially in the light of later records. At 2 P.M. the ventricular rate was 149 beats per minute and regular (Fig. 1-4). This record shows the aberrant nature of the ventricular complexes to be less marked than in previous records. (No quinidine sulphate was given on May 18.)

Two hours later another record (Fig. 1-5) disclosed the same type of ventricular complex as in Fig. 1-4. However, there was a definite irregularity in the rhythm due to an interpolated ventricular beat (Fig. 1-5X) which resembled the other ventricular complexes in this lead. The ventricular rate is doubled by the interposition of this beat. This is further evidence that we may be dealing here with an auricular flutter with a 2:1 response interrupted in this one instance by a 1:1 response of auricle to ventricle. The aberrant nature of the ventricular complexes may be due to quinidine intoxication, since they disappeared after quinidine was discontinued. However, we cannot definitely rule out the possibility of an ectopic ventricular tachycardia.

Subsequent Course.—The ventricular rate on the evening of May 18, 1933 (tenth day), again increased to 180 beats per minute and throughout the night ranged from 180 to 220 beats per minute. No quinidine sulphate had been given this day. The patient again went into circulatory collapse. Early the next morning (May 19) the ventricular rate fell to 100-120 beats per minute, and the patient's condition im-

proved. Later that day she could dimly see moving objects. Toward evening a left homonymous hemianopsia was found. On the following day (May 20) the patient's visual fields became larger and gradually increased until they again were normal. The ventricular rate remained at 100-120 until May 23, when moderate doses of digitalis were again administered and fibrillation of the auricles resulted, although digitalization before the quinidine sulphate had been administered had not altered the rhythm. The ventricular rate was now maintained at 80-100 beats per minute by the administration of large daily doses of this drug for four weeks, when the paroxysms of 1:1 flutter returned at irregular intervals.

SUMMARY

A woman with hypertension and repeated paroxysms of 1:1 auricular flutter received 20.8 grams of quinidine sulphate within nine days, in total doses ranging from 0.4 gram to 4.8 grams a day with the purpose of abolishing this abnormal rhythm.

The doses ranged from 0.2 gram of the drug at two hour intervals to 0.4 gram at hour intervals. On the fourth day, after 9 grams of quinidine had been administered, the auricular flutter was temporarily abolished and normal sinus rhythm was restored for a few hours. Following the reestablishment of auricular flutter, the patient went into circulatory collapse on several occasions when there was a return of the 1:1 flutter.

A ventricular rhythm with widely aberrant complexes resembling those seen in ectopic ventricular tachycardias was found on the ninth day, and the drug was then discontinued. All these abnormal complexes then disappeared. On the tenth day, one day after the drug had been discontinued, the patient complained of blindness which gradually disappeared, and normal vision returned after four days.

Department of Reviews and Abstracts

Selected Abstracts

Simmons, Stanley T.: Rheumatic Heart Disease: Clinical Data as Observed in Louisville, Kentucky. Am. J. M. Sc. **187:** 773, 1934.

In this study of 206 cases of rheumatic heart disease seen in the Louisville City Hospital, it was noted that the disease occurred most commonly in the third and fourth decades of life. The sex incidence showed the usual greater frequency of infection in females in the ratio of 3:2. There was a predominance of white patients to colored in the ratio of 5:3. There was a definite history of rheumatic infection in 91 per cent; 68 per cent of the patients had had rheumatic fever. The first attack occurred before the age of thirty years in 93.5 per cent. The primary infection occurred in only one patient after the age of forty. Seventy-five per cent of the patients were in the hospital some time during the period covered by the study with cardiac symptoms. Eighty-five per cent showed some degree of decompensation before the fortieth year.

Weinstein, A. A.; Davis, David; Berlin, D. D.; and Blumgart, H. L.: The Mechanism of the Early Relief of Pain in Patients With Angina Pectoris and Congestive Failure After Total Ablation of the Normal Thyroid Gland. Am. J. M. Sc. **187:** 753, 1934.

Observations on the immediate postoperative relief of chest pain after total thyroidectomy in nineteen patients are described.

Data were collected before, immediately after, and during several weeks after operation in three groups: (1) changes in nonanginal precordial pain; (2) changes in areas of skin hyperesthesia and muscle and periosteal hyperalgesia of the chest wall; (3) changes in the character and distribution of pain of angina pectoris.

Within a few hours after operation, nonanginal precordial pain, hyperalgesia, and hyperesthesia disappeared, remained absent from two to four weeks but then usually reappeared if the basal metabolic rate had not declined significantly. Only after the basal metabolic rate had dropped appreciably did the above mentioned signs and symptoms diminish or disappear permanently.

Studies were made on the distribution of the pain of angina pectoris produced under standard conditions in three patients before and after hemithyroidectomy. The remaining half of the thyroid gland was removed at a later date. Exercise within two weeks after hemithyroidectomy produced no pain in the arm and the side of the chest corresponding to the side of operation. The pain of angina pectoris was experienced only on the unoperated side and usually stopped sharply at the midline of the sternum. The similarity of these findings to those after cervical sympathectomy and alcohol injection is discussed. The basal metabolic rate did not change appreciably after the first hemithyroidectomy. After from two to eight weeks, pain on exercise was again experienced on the operated side.

Only after removal of the other half of the thyroid gland and after an appreciable drop in the basal metabolic rate was the pain of angina pectoris permanently relieved.

These observations point definitely to the following conclusions: (1) the immediate relief of pain after total thyroidectomy is due to the interruption of afferent nerve impulses from the heart at the time of operation; (2) relief by this mechanism is only temporary; (3) permanent relief is related to the lessened work of the heart attendant on the development of the hypothyroid state.

These findings indicate that after total ablation of the thyroid, complete bed rest should be enforced, despite the early subjective relief experienced by the patient, until the basal metabolic rate shows significant lowering.

Stroud, William D.; Bromer, Albert W.; Gallagher, J. Roswell; and Vander Veer, Joseph B.: A Clinical Comparison of a Purified Glucoside and Whole Leaf Preparations of Digitalis. Am. J. M. Sc. **187:** 746, 1934.

The present study was undertaken in an effort to determine whether or not there is any difference in the therapeutic value of whole leaf as compared with a purified glucoside preparation of digitalis. Twenty-five ambulatory cases of established auricular fibrilation were divided into three similar groups. One group was given a preparation of the extracted, purified glucosides of digitalis; another was given a whole leaf preparation manufactured by a well-established pharmaceutical house; and the third group received whole leaf tablets prepared by the American Heart Association. The groups were followed clinically for nine months and then, after interchanging the preparations, for another period of six months. No significant difference could be ascertained in the clinical pictures of the patients in the three groups during the period of observation.

The Etiology of Acute Rheumatism and Chorea in Relation to Social and Environmental Factors. Joint Discussion of the Section on Epidemiology and Section for the Study of Disease in Children. Proc. Roy. Soc. Med. **27:** 953, 1934.

This discussion by various speakers presents briefly the current ideas on the etiology of rheumatism and chorea in relation to many social and environmental factors. It summarizes briefly, especially the English viewpoint, the many obscure and debatable points in connection with this disease. Several important observations not otherwise reported are included in the discussion.

Pomerance, Max, and Frucht, Simon: Heart Block in Rheumatic Fever. Am. J. Dis. Child. **47:** 1087, 1934.

In a series of children with rheumatic fever, thirty-one in number, twenty-eight showed prolongation of the P-R interval; the other three showed complete dissociation, complete heart-block and left bundle-branch block, occurring during the acute attack. These three cases illustrate four important considerations of these disturbances of cardiac rhythm: (1) the fleeting character of the abnormal rhythm; (2) the accelerated ventricular rate in complete heart-block, making the clinical diagnosis impossible; (3) the curious auriculoventricular dissociation in which the ventricular rate is higher than the auricular rate; (4) the necessity for exact records in all rheumatic cases.

Siemsen, Walter J.: Evaluation of Nonorganic Auscultatory Cardiac Findings and the Venous Hum in Children. Am. J. Dis. Child. **47:** 1100, 1934.

Healthy boys attending the University of Chicago laboratory schools and ranging in age from five to eighteen years served as subjects for the observations reported. Except for the exclusion of children with abnormal cardiac findings

or with physical incapacitation and except for the omission of cases because of incomplete data, the material was unselected. Observations were made during the routine annual examinations, the boys thus being unaware of any unusual proceedings. Observations were made on the incidence of arrhythmias, the incidence of third heart sounds, reduplicated heart sounds, functional heart murmurs, murmurs produced by exercise, and the venous hum.

On the basis of the evidence accumulated, the author attempts to point out the insignificance of presumably nonorganic auscultatory cardiac findings as commonly encountered. While the inconsequential nature of the phenomena has been stressed, emphasis on due care in their proper evaluation has been omitted.

Neiman, Benjamin H.: Verrucous Aortitis With Special Regard to Aneurysm Formation in Children. J. Lab. & Clin. Med. **19:** 929, 1934.

In a series of 4,100 consecutive autopsies, 3 cases have been found in which there was a verrucous lesion on the intima of the aorta. In one case which was associated with a stenosis of the isthmus, the verrucous aortitis had caused a spontaneous rupture of the aorta in an eleven-year-old child. In another, a four-year-old child, an aneurysm of the aorta developed on the basis of it and ruptured into the pericardial sac. Streptococci were demonstrated in this case.

The formation of the verrucae is explained on the basis of a fibrinoid swelling and necrosis of the ground substance of the intima with proliferation of the adjacent fibrocytes. The rupture and aneurysm are explained on the basis of necrosis destroying the internal elastic membrane with subsequent weakening of the media. The nonspecificity of the verrucous lesion of the intima of the aorta is pointed out.

Friedberg, Charles K., and Gross, Louis: Periarteritis Nodosa (Necrotizing Arteritis) Associated With Rheumatic Heart Disease. Arch. Int. Med. **54:** 170, 1934.

Four cases that came to autopsy are presented in which widespread periarteritis nodosa was associated with rheumatic fever and rheumatic heart disease; the latter was confirmed by the presence of Aschoff bodies in the myocardium. These four were discovered in a series of eight cases of periarteritis nodosa which came to autopsy in the course of two years. Prior to this period there were five additional cases which came to autopsy. Two of the five patients had a rheumatic history and evidence of rheumatic valvular disease. Verrucous endocarditis was disclosed in both cases at postmortem examination.

Criteria for the diagnosis of rheumatic infection and of periarteritis nodosa are discussed. On the basis of these criteria, none of the cases of periarteritis reported in the literature presented adequate evidence of rheumatic heart disease. Conversely, none of the vascular lesions described in rheumatic fever could be truly called periarteritis nodosa. Because of the frequency of the association of these diseases in this series and the simultaneous occurrence of the symptoms of each, it is believed that rheumatic fever is probably a common cause of the vascular lesions termed periarteritis nodosa.

In two of the cases an attack of scarlet fever occurred eight weeks before the symptoms of the other ailments became manifest. This point is briefly discussed. In another case there was clinical and pathological evidence of malignant sclerosis. This is mentioned in connection with Fahr's belief that rheumatic fever is one of the causes of malignant sclerosis. In two of the cases the abdominal symptoms, so common in periarteritis nodosa, dominated the clinical picture sufficiently to lead to an exploratory operation. It is suggested that when acute abdominal symptoms

are present in a patient suffering from rheumatic fever, complicating periarteritis nodosa should be considered. This complication is offered as an organic basis for some of the instances of so-called abdominal rheumatism.

Campbell, Maurice: The Respiratory Exchange During Exercise in Heart Disease. Quart. J. Med. 3: 369, 1934.

In patients with heart disease, the percentage increase of the pulmonary ventilation during easy exercise was normal. The increase took place more slowly at the beginning and lasted longer afterward. At rest the ventilation was rather greater relatively to their size, and this remained true during and after exercise.

The breathing was faster and more shallow, especially during exercise. This rapid shallow breathing was more characteristic of mitral stenosis and of those who were most breathless. The effective alveolar ventilation was therefore a smaller percentage of the total pulmonary ventilation. Both these factors would tend to cause dyspnea, but alone they would not do so in a normal subject.

In spite of the shallow breathing the percentage of the vital capacity which was needed, even during these easy exercises, was greater than normal (33 against 20 per cent). No doubt this was an important factor in the sensation of breathlessness.

The percentage of carbon dioxide in the expired air was lower than normal, and this difference was increased during exercise, especially in those with mitral stenosis, and in those who were short of breath with easy walking.

The output of carbon dioxide, especially in the first minute of exercise, was less than normal, and this lag would be responsible for some degree of hyperpnea during the remainder of the exercise and after. The utilization of oxygen was almost the same as normal, and the oxygen debt at the end of exercise was less than this retention of carbon dioxide. The pulmonary ventilation and the intake of oxygen did not differ greatly from the normal in these patients with heart disease.

It seems probable that the more rapid shallow breathing with a smaller effective alveolar ventilation and the lower percentage of carbon dioxide expired were factors in the production of their dyspnea. But the smaller margin between their depth of breathing and their maximum vital capacity appeared a more important factor in their sensation of dyspnea.

Gilchrist, A. Rae: The Effects of Bodily Rest, Muscular Activity and Induced Pyrexia on the Ventricular Rate in Complete Heart Block. Quart. J. Med. 3: 381, 1934.

The ventricular rate in complete heart-block is not fixed but under conditions of bodily rest fluctuates through a range of rate more or less peculiar to the individual.

Clinically it was possible to divide these cases into broad groups—a degenerative and a "toxic" variety. The coefficient of correlation between the auricular and the ventricular rates is less perfect in the "toxic" than in the degenerative group, indicating a more labile regulation of the independent rhythms in the former.

Muscular exercise increases the rate of ventricular beating in complete heart-block. A simple test, consisting of repeatedly climbing a height of 1.5 feet in a given time, induced a maximum increase of 50.2 beats per minute in one patient and a minimum of 1.2 beats in another. The power to increase the rate of ventricular beating in response to exertion varies considerably in different individuals. Similarly the rate of the recovery process is inconstant. In some patients the ventricles return to their preexisting rate within one minute of completing the test; in others three, four or five minutes may elapse before the rates become fully readjusted to resting conditions.

The maximum natural range in auricular and ventricular rates has been estimated by taking the difference between the rate recorded immediately after exercise and the minimum rate observed in a series of observations for each individual under conditions of prolonged bodily rest. The maximum range in rate varies in different subjects, and the maximum auricular and ventricular ranges are not of the same order of magnitude.

In this series of cases it is found that the maximum auricular and ventricular ranges vary inversely. A range of 150 per cent in auricular rate is accompanied by only 10 per cent in ventricular; a 50 per cent gain in auricular rate coexists with a 100 per cent gain in ventricular. In other words, the greater the limitation in ventricular range the more labile the auricular. The greater the ventricular range the less incapacitating are the cardiac symptoms. In complete heart-block an important factor in promoting myocardial efficiency is the ability to quicken the ventricular rate in response to the demands of physical exertion.

In three patients it was found that during sleep the ventricular rate was slower than that recorded under similar conditions awake.

Fever increases the rate of ventricular beating in complete heart-block. In the course of the "protein-shock" reaction a rise of 1° F. may account for an increase of about four beats per minute in the rate of the ventricles.

These observations suggest that functionally there is no essential difference between the sino-auricular node and the idioventricular center. Each reacts to similar forms of stimulation, but the magnitude of the responses would appear to be limited chiefly by the natural differences in the rhythmicity of the two centers of impulse production.

Richards, Dickinson W., and Barach, Alvan L.: Prolonged Residence in High Oxygen Atmospheres. Effects on Normal Individuals and on Patients With Chronic Cardiac and Pulmonary Insufficiency. Quart. J. Med. 3: 437, 1934.

Two normal men and twenty-eight patients in the cardiac insufficiency state have been kept in atmospheres of from 40 to 50 per cent oxygen for continuous periods ranging in length from five days to seven months. Studies have been made in these subjects, of the effects of high oxygen atmospheres upon circulatory and pulmonary functions, and in certain instances upon their water and electrolyte balances.

Two normal subjects residing for a week in 45 per cent oxygen showed a fall in pulse rate, a slight rise in blood CO_2 levels, no appreciable change in respiratory metabolism, in cardiac output, or in excretion of electrolytes or water.

The response to high oxygen atmosphere in favorable cases of congestive heart failure was found to follow a fairly definite pattern or sequence of events.

(a) Dyspnea and restlessness were partly relieved within a few hours, but completely relieved only after several days.

(b) Arterial oxygen saturation was restored to normal or raised slightly above normal within the first twenty-four hours. Rise in blood CO_2 began on the first day, then continued progressively for several days.

(c) Increase in urinary chloride and water excretion frequently occurred, beginning from one to six days after the beginning of oxygen treatment, then proceeding to complete loss of edema.

The favorable response to prolonged oxygen treatment was found to be similar in general course to the recovery of compensation by other means, though definite differences in certain details were encountered. These have been further discussed.

Of twelve cases of arteriosclerotic heart disease, severely decompensated, eight patients were restored to limited ambulatory activity, following prolonged oxygen

treatment, three were temporarily improved, one was not improved. Eight out of nine patients with edema had a diuresis during their course in high oxygen.

Of nine patients with rheumatic heart disease severely decompensated, none was restored to ambulatory activity. Five patients showed moderate improvement and relief of symptoms; the remaining four were not appreciably improved.

Of five patients with pulmonary fibrosis with secondary circulatory insufficiency, all were improved. Two were restored to ambulatory activity.

The clinical indications for oxygen therapy in relative order of importance, are: (a) dyspnea; (b) restlessness; (c) cardiac pain of anginal type; (d) arterial oxygen unsaturation; (e) cyanosis; (f) cough.

Cowan, Donald W.: The Creatine Content and the Weight of the Ventricles in Experimental Hyperthyroidism and After Thyroparathyroidectomy. Am. J. Physiol. **109**: 312, 1934.

The present investigation was undertaken to determine the effect of both hyper- and hypothyroidism upon the creatine concentration as well as the total amount of creatine in the ventricles of experimental animals. Young adult male rats were used in this work.

Thyroxine whether administered in divided doses over a period of time or in a single large dose causes an actual increase in ventricular muscle mass (in spite of a lowering of general body weight). There is a decrease in creatine concentration in the ventricles and an actual loss of creatine from the heart.

Thyroparathyroidectomy while producing no change in the weight of the ventricles does cause a slight but significant loss of creatine from the heart.

Nathanson, M. H.: Further Observations on the Effect of Drugs on Induced Cardiac Standstill. Arch. Int. Med. **54**: 111, 1934.

In certain persons the activity of the cardiac pacemaker may be temporarily eliminated and an arrest of the heart induced by pressure on the right carotid sinus. In eight cases studied, the subcutaneous injection of epinephrine abolished the standstill by stimulating a new center of impulse formation in the ventricles. Ephedrine administered intravenously produced a similar response in three cases. Barium chloride by mouth abolished the cardiac standstill in a similar manner in one case and was ineffective in another. Calcium gluconate, caffein sodium benzoate, coramin metrazol and thyroxine were without effect in a subject who responded consistently to epinephrine. Digitalis prolonged the period of induced cardiac standstill. A group of compounds chemically related to epinephrine produced in a varying degree a reaction similar to that of epinephrine. The ratio of activity of these compounds as compared with epinephrine was estimated.

The effectiveness of the epinephrine-like compounds indicates that in the therapy of cardiac standstill a specific pharmacodynamic action is required, which is the stimulation of the cardiac accelerator mechanism.

Epinephrine is the most active drug in the treatment of the stopped heart and in the prevention of the frequent syncopal attacks of chronic heart-block.

Harrison, T. R.: Friedman, Ben; Clark, Gurney; and Resnik, Harry: The Cardiac Output in Relation to Cardiac Failure. Arch. Int. Med. **54**: 239, 1934.

The cardiac output of patients with cardiac disease has been studied by the acetylene method, modified in such a way as to allow the detection of inaccurate results. The cardiac output per minute of patients with congestive heart failure

is usually from 10 to 30 per cent less than that of normal subjects but may be within the normal range. Patients without circulatory disorders may have an equally low cardiac output. The level of the cardiac output per minute, whether considered as such or in relation to the metabolic rate, bears no relation to the presence or absence of congestive failure for:

1. The range and the average values of the cardiac output are similar for compensated and decompensated patients.

2. In a given individual, clinical improvement and disappearance of congestive phenomena may be associated with an increase, a decrease or no change in this function. In general, the output of the heart per beat tends to be somewhat less during congestive failure. The metabolic rate is normal in some patients and elevated in others.

These observations are interpreted as indicating that the "forward failure" (diminished output) hypothesis, which ascribes the clinical manifestations of congestive heart failure to an insufficient supply of blood to the tissues, is erroneous. The "backward failure" (back pressure) theory has been discussed, and it is concluded that there is much evidence in favor of it and no valid evidence against it.

Thompson, H. E., and Dragstedt, C. A.: Modifying Action of Calcium and Sodium Bicarbonate of Salicylate Intoxication. Arch. Int. Med. **54**: 308, 1934.

Experiments on normal healthy dogs were undertaken to determine whether a mixture of calcium salt with acetyl salicylic acid would be less toxic than acetyl salicylic acid alone. The amount of the drug used was large enough to correspond to an intensive type of salicylate medication employed clinically for short periods to accomplish what may be called salicylization.

The ameliorating effect of sodium bicarbonate on certain of the untoward symptoms produced by salicylate medication in these amounts reported by many workers is confirmed by these experiments. Simultaneous administration of calcium in the form of calcium gluconate and acetyl salicylic acid was found to have a similar and in certain respects, a greater ameliorating effect.

Meeker, Dorothy R., and Jobling, James W.: A Chemical Study of Arteriosclerotic Lesions in the Human Aorta. Arch. Path. **18**: 252, 1934.

Analysis of arteriosclerotic plaeques after careful isolation of the portions involved in intimal lesions apart from other portions of the aorta from forty-five patients showed a constant amount of phospholipids, an increase of total fatty extract and total cholesterol particularly in the proportion of cholesterol to total fatty extract. This increase apparently becomes greater with increasing severity in the lesions rather than with increasing age. The study also showed that as the severity of the lesions increases, there is first an increase in percentage of cholesterol esters, in a fatty extract and then as the process continues, a decrease.

Bellet, Samuel, and Johnston, Charles G.: The Effect of Coronary Occlusion Upon the Initial Phase of the Ventricular Complex in Precordial Leads. J. Clin. Investigation **13**: 725, 1934.

In acute experiments upon dogs and cats ligation of the anterior descending branch of the left coronary artery, while causing R-T deviation in precordial leads, produced practically no change in the initial downward deflection of the ventricular complex. In general, ischemia or damage to a much greater portion of the myocardium than that supplied by the anterior descending branch of the left coronary artery was required to produce a marked diminution or disappearance of the initial downward deflection. Diminution or disappearance of this deflection was produced in cats

after ligation of the anterior branch of the left coronary plus the anterior branch of the circumflex arteries, or in dogs and cats after cauterization of a considerable portion of the surface of the cardiac muscle.

In survival experiments marked diminution or disappearance of the initial downward deflection could be produced by ligation of the anterior descending branch of the left coronary artery alone. In 3 out of 5 dogs this deflection almost completely disappeared from twenty-four to forty-eight hours after ligation. In one cat it disappeared two hours after operation. In one dog it was markedly diminished on the fifth day after operation and in another moderately diminished on the third day. In all 5 dogs, later during the recovery stage, it increased again; in one instance the return was complete; in the remaining 4 the deflection regained one-fourth to one-half its original amplitude. In man the initial downward deflection which disappears during the acute stage of infarction usually does not return in the chronic stage; occasionally, however, a partial return occurs. The return of this deflection in the dog is probably to be explained by the smaller relative size of the area involved by the chronic infarct and by the larger portion of the left ventricle in relation with the anterior chest wall in the dog.

Extremely tall T-waves observed in these experiments as a transient phenomenon are believed to characterize a subacute stage of infarction.

Ligation of the coronary arteries supplying the posterior wall of the left ventricles or injury of this area by cauterization produced R-T interval deviations above the isoelectric line but no change in the amplitude of the initial downward deflection.

Gilligan, D. R.; Berlin, D.D.; Volk, M. C.; Stern, B.; and Blumgart, H. L.: Therapeutic Effect of Total Ablation of Normal Thyroid on Congestive Heart Failure and Angina Pectoris. IX. Postoperative Parathyroid Function. Clinical Observations and Serum Calcium and Phosphorus Studies. J. Clin. Investigation 13: 789, 1934.

Tetanic convulsions or spontaneous spasm of the extremities did not occur in any of the seventy-three consecutive patients on whom total thyroidectomy was performed. Clinical signs or symptoms of mild parathyroid deficiency were manifest after operation in twelve patients, or 17 per cent, of this entire series. Of the last thirty-seven patients of this group of seventy-three, only three, or 8 per cent, showed signs or symptoms. In ten of the twelve patients clinical signs and symptoms of hypoparathyroidism were transient, disappearing within two weeks. One patient who was operated upon two and a half months previously and another nine months previously still showed signs and symptoms when specific medication was discontinued. The symptoms of hypoparathyroidism are attributed to injury, rather than to removal of parathyroid glands during operation.

Oral administration of calcium chloride solution and a diet rich in milk controlled the symptoms of tetany in most patients in whom the disease was transient. An initial intravenous injection of calcium chloride solution was given to three patients; calcium lactate or gluconate was substituted when oral administration of calcium chloride solution was not tolerated. Viosterol, together with a large intake of calcium, is being employed successfully in the two cases with persistent hypoparathyroidism.

The serum calcium was reduced to 7.5 mg. per 100 c.c. or less in six of the twelve cases at the time of onset of tetany; in three cases the serum calcium was between 8.3 and 8.6 mg. per 100 c.c.; in the remaining three cases the serum calcium was within the accepted normal limits. The values for serum inorganic phosphorus in these patients with early postoperative tetany were usually normal, being 5.0 mg. per cent or above in only two cases.

Appreciable decreases in concentration of serum calcium and no changes in concentration of serum inorganic phosphorus were observed during the first two weeks after total thyroidectomy in a group of patients who showed no clinical signs of insufficient parathyroid function. The concentration of serum calcium was usually slightly below the preoperative level during the first year after thyroidectomy, both in those individuals who showed transient signs and symptoms of hypoparathyroidism soon after operation and in patients who showed no clinical signs of this disorder at any time.

It is pointed out that the chemical changes in the blood present during the early stages of postoperative tetany may be quite different from the characteristic markedly low serum calcium and high phosphorus values found in chronic hypoparathyroidism of either idiopathic or postoperative origin.

The transient tetany which sometimes occurs immediately following total thyroidectomy can be controlled by calcium therapy; persistent parathyroid insufficiency occurs so rarely that it does not constitute a contraindication to total thyroidectomy.

Pwelow, S., Markle, P., and Katz, L. N.: Factors Involved in the Production of Skeletal Muscle Pain. Arch. Int. Med. 53: 814, 1934.

The results of this study show that the immediate cause of continuous muscular pain such as occurs when an ischemic muscle is exercised is not produced by a single mechanism but that muscular activity, anoxemia, circulatory stasis and possibly other processes contribute to its production.

Ernstene, A. Carlton, and Snyder, Maurice: Effect of Arteriosclerosis and Benign and Malignant Hypertension on the Area of Histamine Flares. Arch. Int. Med. 53: 865, 1934.

The area of flare produced by injecting 0.02 c.c. of a 1:2,000 dilution of histamine dihydrochloride into the skin of the mid forearm was measured in five groups: normal persons, patients with arteriosclerosis and normal blood pressure, patients with benign essential hypertension, patients with hypertension of the intermediate grade, and patients with malignant hypertension. In eleven of the sixteen patients with malignant hypertension, the area of flare was less than the smallest recorded in a normal person, while in only three did it exceed 24 sq. cm. The average area for the group was 16 sq. cm., approximately one-half that of normal persons.

The results of the investigation indicate that observations on the area of the histamine flare should prove a useful adjunct in distinguishing the intermediate and malignant types of hypertension from the benign form.

Allen, Edgar V., and Camp, John D.: The Value of Arteriography. Radiology 22: 678, 1934.

The roentgenographic studies in a case of thromboangiitis obliterans indicate not only the diagnostic value of arteriography but also the powers of compensation for disease which are inherent in the arterial system.

The chief value of arteriography in the authors' estimation lies not in the direction of diagnoses but in determining the pathogenesis of the condition. It gives information of inestimable value regarding the disturbances in the arterial circulation in scleroderma, thromboangiitis obliterans, in aneurysms, arteriovenous fistulas and arterial emboli. Whether or not the method will add information of value to knowledge of pathogenesis of arthritis, hypertension and of other conditions remains to be learned in the future.

Clark, Janet H., Hooker, Donald R., and Weed, Lewis H.: The Hydrostatic Factor in Venous Pressure Measurements. Am. J. Physiol. **109**: 166, 1934.

Direct measurements of the venous pressure in dogs in the horizontal and two vertical (head-down, head-up) positions have shown that the heart is not the point from which the hydrostatic factor in venous pressure is measured. In the dead animal the venous system acts as an unbroken column from head to tail, and the reference point from which hydrostatic pressure is measured was found to be 82 mm. caudal to the heart in the vertical position in an animal of approximately 500 mm. spinal length. In the living animal the venous system is broken at the heart, giving two columns with a reference point approximately 121 mm. from the heart in the tail section and another reference point 38 mm. from the heart in the head section.

Kovacs, Joseph: The Iontophoresis of Acetyl-Beta-Methylcholin Chlorid in the Treatment of Chronic Arthritis and Peripheral Vascular Disease. Am. J. M. Sc. **188**: 32, 1934.

A preliminary report on the action of the iontophoresis of acetyl-beta-methylcholin chlorid is presented.

Acetyl-beta-methylcholin chlorid introduced locally with the help of the galvanic current produces a pronounced and prolonged local effect which cannot be obtained through subcutaneous or oral administration. This local treatment appears to be of value in chronic arthritis especially in the rheumatoid type. This treatment may also be of value for patients with peripheral vascular disease in which spasm is an important factor. No harmful effects were observed.

Further studies with prolonged observation of cases, especially in view of the fallacies lurking in the evaluation of the therapeutic test, are essential for the correct evaluation of this method.

Bruen, Curtis: The Therapeutic Efficacy of Bismuth Subnitrate in Arterial Hypertension. Am. J. M. Sc. **188**: 21, 1934.

Under the conditions established for experimental observation, it was determined that bismuth subnitrate by mouth even in the largest therapeutically practicable doses does not develop sufficient nitrate action to exert any demonstrable effect on the blood pressure or symptoms of arterial hypertension.

Nadler, J. Ernest; Green, Henry; and Rosenbaum, Arthur: Intravenous Injection of Methylene Blue in Man With Reference to Its Toxic Symptoms and Effect on the Electrocardiogram. Am. J. M. Sc. **188**: 15, 1934.

These observations indicate that methylene blue under the conditions of this study has two actions. The first of these is the oxidation of hemoglobin to methemoglobin. The amount of methemoglobin found immediately following the injection of the average therapeutic dose is small.

The second is that this drug, used intravenously, excites the individual and by its rapid elimination into the stomach and urine produces transitory gastrointestinal and urinary irritation. The most frequent toxic symptoms observed were restlessness, paresthesias, a sense of "burning" in the mouth and stomach, pain in the chest, and strangury. These manifestations usually subsided in from twenty-four to forty-eight hours. Leakage of a small amount of methylene blue about the vein gives rise to a very painful infiltration.

Electrocardiographic studies show that methylene blue produces a reduction in the height or even reversal of the T-wave frequently with lowering of the R-wave. This suggests depression of the ventricular musculature.

The amount of methemoglobin found and the subsequent decrease in hemoglobin is not of sufficient magnitude to account for the clinical picture described on the basis of anoxemia.

The authors wish to point out, therefore, that the indiscriminate use of methylene blue may produce unpleasant results and be dangerous to the patient.

Harrison, T. R.; King, C. E.; Calhoun, J. A.; and Harrison, W. G., Jr.: Congestive Heart Failure. XX. Cheyne-Stokes Respiration as the Cause of Paroxysmal Dyspnea at the Onset of Sleep. Arch. Int. Med. 53: 891, 1934.

A pneumographic study has been made of patients complaining of attacks of dyspnea coming at the onset of sleep. Such patients exhibit Cheyne-Stokes respiration which either appears or becomes more marked at the onset of sleep and later during deep sleep either disappears or becomes less marked. As sleep develops, respiratory periodicity occurs with increasing length of the apneic intervals and a corresponding increase in the intensity of the hyperpneic phase, which eventually becomes so marked as to awaken the patient and cause dyspnea.

An investigation has been made concerning the underlying factors responsible for these phenomena, and it is concluded that the main causative agents are: overventilation due to reflex respiratory stimulation from congested lungs and respiratory depression occurring at the onset of sleep. Acting singly or in combination, these two physiologic alterations appear to be responsible for the periodic breathing. The associated violet hyperpnea in a patient with diminished vital capacity is responsible for the subjective respiratory distress.

Certain observations on the blood gases before and during sleep have been presented, and these are compatible with the hypothesis mentioned. The development of periodic breathing is usually not associated with significant alterations in the composition of the blood. As sleep continues there is, however, a demonstrable increase in the carbon dioxide tension and in the acidity of the blood, and coincidentally the respiration becomes regular.

The alterations in the blood gases are primarily effects of the changes in breathing. However, as a result of the alteration in the blood, the breathing undergoes further changes which lead to the production of the characteristic paroxysmal seizures of respiratory distress.

Friedman, Ben, Clark, Gurney, and Harrison, T. R.: Studies in Congestive Heart Failure. XXII. A Method for Obtaining "Mixed" Venous Blood by Arterial Puncture. J. Clin. Investigation 13: 533, 1934.

A modification of the method of Burwell and Robinson for determining the gas contents of "mixed" venous blood has been described. The procedure depends on obtaining blood from a peripheral artery while the subject breathes a gas mixture which has been equilibrated with his venous blood by previous repeated rebreathings.

The several procedures involved in the method have been checked by various experiments.

Application of the method to dogs has demonstrated that the values found for the blood gases by this indirect method are in close agreement with the gas contents of blood obtained by puncture of the right ventricle. The presence in the lungs of sufficient fluid to produce well-marked arterial anoxemia does not invalidate the results.

The method is difficult to employ and involves considerable discomfort to the subject. Its agreement with the modified acetylene procedure constitutes additional evidence as to the validity of the latter in subjects with cardiac disease.

Harrison, T. R., Calhoun, J. A., and Harrison, W. G., Jr.: Congestive Heart Failure. XXI. Observations Concerning the Mechanism of Cardiac Asthma. Arch. Int. Med. 53: 911, 1934.

Cardiac asthma has been defined and has been differentiated from other types of paroxysmal and nocturnal dyspnea occurring in patients with cardiac disease. The dyspnea of cardiac asthma is not usually associated with abnormalities in the oxygen, carbon dioxide or hydrogen ion content of the arterial blood.

Relief of the seizure of morphine is not associated with constant alteration in the gases of the blood but is followed by a decrease in ventilation and is usually accompanied by an increase in vital capacity.

Pulmonary congestion, with its twofold effect of decrease in vital capacity and reflex respiratory stimulation, is always present and appears to be the underlying cause of cardiac asthma.

There are a number of different precipitating causes of the seizures. Of these, cough is the most common. Less frequently, fear—produced by unpleasant dreams—abdominal distention or warmth may precipitate the seizures. Each of these precipitating factors appears to act by increasing the ventilation. It has been shown that, both in normal persons and in patients with cardiac disease, an increase in ventilation is accompanied by a rise in consumption of oxygen, which occurs immediately and thereby indicates that the cardiac output is also increased.

The effects of voluntary overventilation on the vital capacity were studied in normal subjects and in patients with left ventricular failure. The former persons usually had a slight rise in vital capacity, but the reverse effect was usually obtained in the patients.

A typical seizure of cardiac asthma was produced in one patient by voluntary overventilation and in another subject by voluntary coughing.

Acute pulmonary edema causes both chemical and reflex stimulation of breathing and may thus accentuate dyspnea. It has also been shown that in dogs "edema" of the lungs produced by introducing Ringer's solution may cause marked anoxemia with a consequent increase in the cardiac output.

It has been shown that patients dying with congestion of the lungs may have a noninflammatory edema of the bronchial walls, and this is believed to be responsible for the musical and sonorous râles which are often heard during the dyspneic seizures. Thus, an "obstructive" dyspnea may be superimposed on a "reflex" dyspnea.

The occurrence of the attacks during sleep appears to be dependent on the depressed irritability which allows the various stimuli mentioned to become excessive before they awaken the patient. On awakening there is marked increase in breathing because of the sudden increase in irritability of the respiratory center, plus the strong stimulus. The resulting increase in ventilation tends to cause additional pulmonary congestion which leads to further increase in ventilation. The vicious cycle so started may progress to acute pulmonary edema unless it is broken by the patient's assuming the upright posture, by the administration of morphine or by removal of the precipitating cause, i.e., expectoration of mucus, relief from fear of nightmares, etc.

The same factors which cause cardiac asthma by night may cause seizures during the day and result in more or less continuous dyspnea.

Four types of nocturnal dyspnea occur in patients with cardiac disease; these are orthopnea, evening dyspnea, Cheyne-Stokes respiration and cardiac asthma. They

all have a common underlying cause, namely, pulmonary congestion consequent to "back pressure" from the left side of the heart.

Starr, Isaac, Jr.; Donal, J. S.; Margolies, A.; Shaw, R.; Collins, L. H.; and Gamble, C. J.: Studies of the Heart and Circulation in Disease; Estimations of Basal Cardiac Output, Metabolism, Heart Size and Blood Pressure in 235 Subjects. J. Clin. Investigation **13:** 561, 1934.

Duplicate estimations of cardiac output together with determination of metabolism, blood pressure and pulse rate have been performed on 31 healthy persons and 204 hospital patients under conditions of basal metabolism. Orthodiagrams were secured also. The results have been subjected to statistical analysis.

The cases studied included patients with diseases not affecting the circulation, with hypertension, anemia, hyperthyroidism, neurocirculatory asthenia, valvular heart disease, various types of arrhythmia, coronary disease, acute endocarditis, and aneurysm; also patients who had recovered from congestive heart failure. Acute cardiac decompensation, advanced pulmonary disease, and the febrile diseases were not studied.

The condition of the circulation in the various forms of disease has been described and compared with the normal. The most unexpected finding was that the average basal circulation in cases of neurocirculatory asthenia was very abnormal.

Relationships by which the condition of the heart muscle might be ascertained have been sought for. Among normal persons and patients with normal hearts but abnormal circulation, the relationship between heart work per beat and heart size holds more closely than any other studied. In patients who have been once decompensated this relationship is abnormal almost without exception. It is believed, therefore, that it may be used to define normal myocardial function and to detect myocardial disease. Charts and equations are submitted by which the normality of any case can be decided.

Edwards, Joseph C., and White, Paul D.: A Note on the Incidence of Neurocirculatory Asthenia With and Without Organic Heart Disease. New England J. Med. **53:** 211, 1934.

In an analysis of 5,000 consecutive patients with cardiac symptoms and signs seen in private practice in New England over a period of thirteen years, 687 patients (13.7 per cent) were found with definite neurocirculatory asthenia. Of the 687 cases, 448 (65.2 per cent) were uncomplicated by organic heart disease. One hundred and thirty-five (19.6 per cent) were complicated by organic heart disease, and there were 104 (15.2 per cent) in which neurocirculatory asthenia was present with doubt as to the presence or absence of organic heart changes. Of the 687 patients, 424 (61.7 per cent) were females and 263 (38.3 per cent) were males. Three hundred and fifty-four (51 per cent) of the 687 patients were in the age group from thirty-one to fifty years inclusive.

Of the types of organic heart disease found with neurocirculatory asthenia in our series, rheumatic heart disease was most frequent (44.4 per cent), coronary disease second (21.4 per cent), and hypertensive heart disease third (18 per cent). There was only one case of cardiovascular syphilis.

From this experience, the authors have found that the chances of a patient with symptoms of neurocirculatory asthenia coming to a consulting physician in New England to show no evidence of organic heart disease, are approximately three to one. Even though organic heart disease be present, symptoms may be entirely the result of a complicating neurocirculatory asthenia.

Book Review

L'INFARCTUS DU MYOCARDE. By Eduardo Coelho, Professor of the Faculty of Medicine and Physician to the Hospital of Santa Marta, Lisbon. Masson et Cie, Paris, 1934, 212 pages with 105 figures.

This monograph, published in French, consists of two parts: (1) an electrocardiographic study of experimentally produced myocardial infarction, and (2) a report of 28 clinical cases followed by a discussion of the etiology, clinical symptomatology, electrocardiography including localization, differential diagnosis and prognosis.

In the first part the author gives a satisfactory summary of his own important work on experimentally produced myocardial infarction and reviews the literature up to about two years ago. The advances since that time have been so great, however, that in certain important respects the discussion can scarcely be regarded as abreast of current knowledge.

The second part of the monograph, which deals with the clinical aspects of myocardial infarction, offers at most a minimal contribution. More than 60 pages are utilized for the protocols of the author's 28 cases and their electrocardiograms. The material is not remarkable. This part of the book is not up to the standards of several articles in English on the same subject.

C. C. W.

Errata

In the article by Dr. Max Winternitz, "The Initial Complex of the Electrocardiogram After Infarction of the Human Heart," published in the June issue (Vol. 9, p. 616) and translated from the German, a number of minor errors appear, of which the corrections are given below:

P. 616, lines 29 and 30: We may find a deep Q_3 apart from coronary thrombosis, with simple sclerosis without necrosis, and even as a variation of the normal electrocardiogram with certain rotations of the heart's axis.

P. 618, line 14: . . . the widening of QRS, measuring 0.1 sec. . . .
line 17: . . . R_1 higher, just measuring 9 mm.
line 24: Dr. A. Ghon. . . .

P. 620, line 7: . . . extensive myomalacia of the heart . . .
line 13: The duration of R_1 is unaltered but it has become smaller and splintered, . . .
line 18: Extensive old myomalacia. . . .

P. 621, line 22: . . . he worked steadily, constantly suffering from stenocardia and epigastric pain.

P. 622, line 28: . . . Siemens' oscillograph.

P. 628, line 11: . . . cerebral, coronary and mesenteric vessels, . . .

P. 629, lines 6 and 7: The initial complex shows slight notching in Leads I and III, small R in Leads II and III. . . .

P. 630, line 12: . . . pain which lasted some hours. . . .

P. 632, Legend to Fig. 14 . . . Siemens' oscillograph.

P. 633, line 7: . . . strophanthin, 0.5 mg., . . .

P. 633, line 27: QRS width 0.12 sec.

P. 636, line 12: Cases of idioventricular rhythm . . .

P. 641, line 18: . . . as is shown in their own illustrations.

In the August issue in the article by Robb and Weiss: Page 762, second line, for 2.6 c.c. read 0.26 c.c.